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MYXOMATOUS DEGENERATION CYSTS OF SKIN AND SUBCUTANEOUS TISSUES

ARTHUR R. WOODBURNE, M.D.
DENVER

DURING the early part of this century references to synovial cysts, ganglions, epidermal cysts and the like (this does not refer to epidermal or epidermoid cysts which are produced by epidermal inclusions following puncture wounds and are usually seen on the palmar surface of the hands) were frequently seen in dermatologic literature. The recent references are almost entirely found in surgical literature.

Since dermatologists are frequently called on to advise patients concerning these lesions, it seemed appropriate to review recent developments and report my work at this time. This report is based on the microscopic study of material from 58 cases and roentgen ray therapy in 105 cases.

Microscopic material was studied from myxomatous degeneration lesions in 38 cases of the wrist, 10 of the hand, 4 of the fingers, 4 of the foot and 2 of the ankle.

The study was originally planned and started in 1937 in conjunction with Dr. R. H. Denham, after a discussion in which I had related the ineffectiveness of surgical treatment of lesions of the fingers and he had reported the equally unsatisfactory results in treatment of the usual ganglions of the wrist. It was our belief that so-called synovial cysts of the fingers and ganglions were essentially the same type of lesions. A review of microscopic material from 58 cases, distributed as indicated, supported our belief. The histologic changes are essentially a cystic cavity in normal dermis or subcutaneous fibrous tissue. The lining wall is made up of flat fibrous tissue cells and shows no endothelial or epithelial lining membrane. There is no inflammatory infiltrate in or about the cavity. The cyst is filled with a clear mucinoid or myxomatous, gelatinous material. Early cysts show first a cystic degeneration of fibrocytes, with droplets of mucinoid material in the

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cytoplasm. These droplets fuse, replace the cell cytoplasm and combine with similar droplets from surrounding degenerating fibrous tissue cells.

King,[1] of Australia, has done some work staining the Golgi apparatus of connective tissue cells, which he felt proved that the mucoid material is produced by the increased secretory activity of fibrocytes returning to embryonal forms because of the stimulation of mild trauma. However, it is my belief as well as that of other observers[2] in this country that the mucoid material is a product of degeneration.

Some observers[3] postulate the mucoid degeneration of a fibroma of the skin or periarticular subcutaneous tissue. A careful review of the history in my cases gave no indication of previously existing solid tumors.

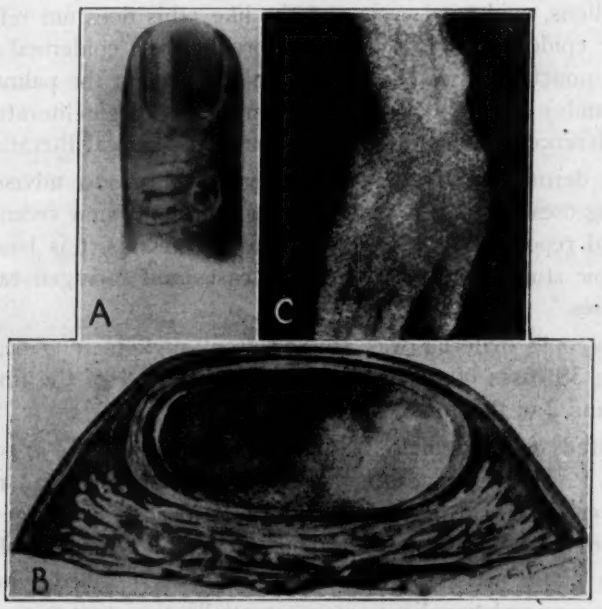

Fig. 1.—*A*, myxomatous degeneration cyst of the finger. *B*, cross section of myxomatous degeneration cyst of the finger. *C*, typical myxomatous degeneration cyst of subcutaneous tissue of the wrist.

Ideas on pathogenesis[4] fall into these main groups: (1) herniation of tendon sheaths, (2) tears of tendon sheaths with lakes of syno-

1. King, E. S. J.: The Formation of Ganglia and Cysts of the Menisce of the Knee, Surg., Gynec. & Obst. **7**:150, 1940.

2. DeOrsay, R. H., and others: Pathology and Treatment of Ganglion, Am. J. Surg. **36**:313, 1937.

3. (*a*) DeOrsay.[2] (*b*) Savatard, L.: Periarticular Fibroma of the Skin ("Synovial" Lesions of the Skin), Arch. Dermat. & Syph. **9**:441 (April) 1924.

4. King.[1] DeOrsay.[2] Savatard.[3b] Gross, R. E.: Recurring Myxomatous Cutaneous Cysts of Fingers and Toes, Surg., Gynec. & Obst. **65**:289, 1937.

vial fluid outside the tendon sheath, (3) secretion of synovial fluid through small channels into surrounding connective tissue, (4) fetal sequestration of synovial membrane, (5) secretory activity of residual embryonic mesenchymal cells or reversions of fibrocytes to more embryonic forms with secretory activity and (6) myxomatous degeneration of fibrocytes.

Adventitious bursas and tendon sheath hernias are occasionally seen and would constitute a major differential diagnostic problem except that the fluid can usually be pressed out from the bursa or hernia back

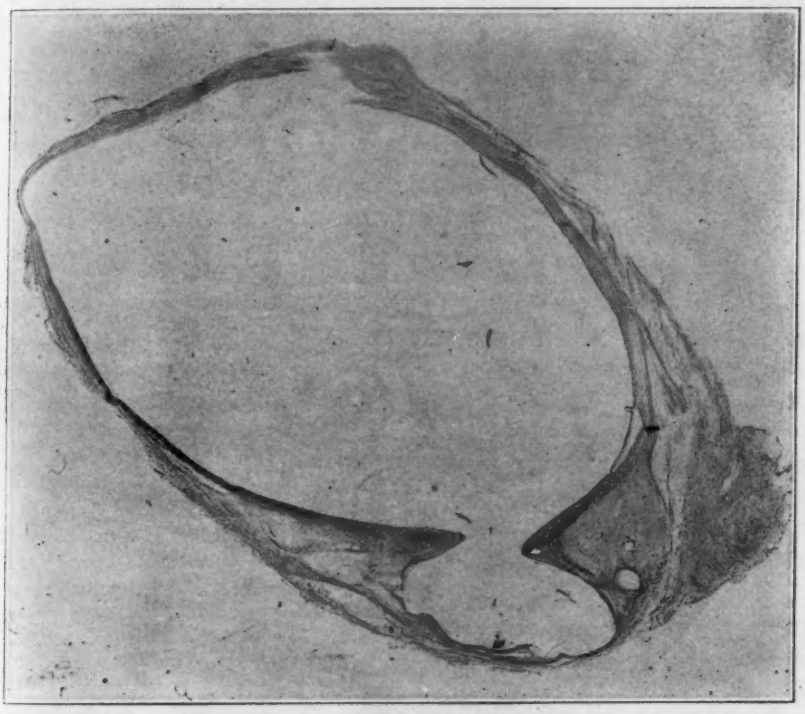

Fig. 2.—Microscopic picture of a cyst from the wrist, showing the multiple lesions which are so frequent.

into the rest of the local synovial system. This should also be true in herniation of tendon sheaths were it tenable. However, microscopic study of serial sections from these lesions shows no evidence to support any of the first four hypotheses since hernias, tears, channels or synovial membrane cannot be found. The recent literature and a critical examination of my patohlogic material make untenable former hypotheses connecting these lesions with any synovial system. Ganglion, since it is merely a gross descriptive term (a hard globular swelling on a

tendon sheath), also is not the best scientific term to apply to the deeper lesions. It is suggested that the name which I have applied to these lesions, myxomatous degeneration cysts, be adopted since it describes the pathologic changes and also gives a more exact idea of the nature of the process.

A review of the literature and the study of my cases have led to the conclusion that myxomatous degeneration lesions, both the former synovial cysts of the fingers and the ganglions of the hands, wrists,

Fig. 3.—High power magnification of a cyst from the wrist, showing absence of lining membrane. The lining is made up of flat fibrocytes.

ankles and feet, are degeneration lesions of fibrocytes in which the cells produce a myxomatous material and in which, by fusion of many small cysts, the clinical lesions, as we know them, are formed.

The location and type of lesions lead to the conclusion that probably friction, pressure and repeated minor trauma are the main factors in the formation of these cysts.

Methods of treatment have been varied and in many instances unreliable in their results. The following list gives some of the common methods used: (1) excision, (2) incision and drainage, (3) excision of the top of the cyst, (4) incision and curettage, (5) chemical cautery with nitric acid, phenol, trichloracetic acid or the like, (6) electrocoagulation, (7) freezing with solid carbon dioxide, (8) injection of proteolytic substances and sclerosing solutions, (9) amputation and (10) roentgen ray or radium therapy.

Needless to say, any lesions in which this number of procedures has been advocated must be resistant to treatment by simple means or one simple effective method would have been generally accepted by this time.

A review of reports of various methods of treatment combined with personal experience may be summarized as follows:

Excision is effective if much surrounding fibrous tissue can be excised. When wide excision is carried out unsightly adherent scars are usual. Incision either alone or with cautery, curettage or drainage is regularly followed by recurrence. Caustics, such as the chemical caustics and solid carbon dioxide, do not destroy the lesion. Electrocoagulation is promptly followed by recurrence.

Ball [5] recommended the injection of the enzyme "caroid" (a proprietary digestant preparation of papau). However, results were uncertain, and soon reports of severe infection were published. Key [6] reported severe infection with sloughing of much tissue. He felt that since "caroid" could not be properly sterilized its contamination with proteolitic bacteria was responsible for his poor results. Injections with sodium morrhuate have been recommended,[7] but have been frequently followed by recurrence. Amputation is effective, but in most cases needlessly radical.

Following the suggestions of Ormsby [8] and Sutton [9] that radium or roentgen ray was most effective in treatment of synovial lesions of the fingers and believing from my pathologic study that ganglions were essentially the same type of lesions, I decided to treat a series of ganglions with roentgen rays.

Five patients were at first treated with suberythema doses, reaction being avoided entirely. Results with this method were entirely

5. Ball, E. J.: A New Method of Treatment of Ganglion, Am. J. Surg. **50**:722, 1940.

6. Key, J. A.: Treatment of Ganglion by the Injection of Caroid a Dangerous Procedure, J. A. M. A. **118**:516 (Feb. 14) 1942.

7. Kaplan, E. B.: Treatment of Ganglion by Injection of Sodium Morrhuate, Am. J. Surg. **24**:151, 1934.

8. Ormsby, O. S.: Synovial Lesions of the Skin, J. Cutan. Dis. **31**:943, 1913.

9. Sutton, R. L.: Radium in the Treatment of Synovial Lesions of the Skin, J. A. M. A. **66**:565 (Feb. 19) 1916.

unsatisfactory in my hands. However, Reeves [10] had recently reported 87 per cent cures with a technic of administering 200 r through 0.5 mm. of copper and with one dose each month. Two, three or four doses have usually been necessary. Lyle [11] has reported 81 per cent cures in 8 cases in which treatment was with a similar technic.

When it was decided that a reaction had to be produced to obtain satisfactory results the dosage was increased and various technics applied.

Ten patients were treated with a peak of 150 kilovolts through 3 mm. of aluminum and two doses of 400 r each, three weeks apart. With this treatment local reaction was limited to slight erythema, and residual atrophy was not seen. Five of the 10 patients had a permanent result. In 5 there was a recurrence, usually within two months, or failure of the cyst to disappear.

Five patients were treated with a peak of 200 kilovolts through 3 mm. of copper and two doses of 400 r each, three weeks apart. Results were no better with the increase in kilovoltage and filtration, so that this method was discontinued.

Ten patients were then treated with a peak of 150 kilovolts through 3 mm. of aluminum, and three doses of 400 r each, one week apart. This group gave a result of 70 per cent cures after three months.

Ten more patients were then treated with roentgen rays, filtered through 3 mm. of aluminum in two doses of 500 r each in one week. In these patients moderate erythema developed, usually followed by some superficial desquamation. The cyst disappeared in all these cases, so that in the balance of the cases treatment was with this technic. In later follow-up in these cases an area of superficial atrophy was seen, with depigmentation and patchy hyperpigmentation. The skin was soft; there was no tenderness, and permanent results were obtained in all cases on the fingers.

In deeper lesions of the wrist, ankle and dorsal surface of the hand and foot there were 80 per cent permanent results.

Disadvantages of the treatment are the resulting area of atrophy, with some depigmentation and patchy hyperpigmentation. In certain cases the production of a small atrophic area is not a too serious sequela.

One of the typical cases is that of a physician's wife, who was a pianist. A nodule developed on the dorsal surface of the left wrist, which was painful if she practiced on the piano for any length of time.

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10. Reeves, R. J.: Radiation Treatment of Ganglia of the Wrist, South. M. J. **37**:584, 1944.

11. Lyle, F. M.: Radiation Treatment of Ganglia of the Wrist and Hand, J. Bone & Joint Surg. **23**:162, 1941.

The lesions had been surgically excised on several occasions, with prompt recurrence. Roentgen ray therapy produced complete relief of pain in a week, with disappearance of the nodule in three weeks.

Occasionally the nodule has failed to disappear for four weeks. Retreatment in a few cases over the same area has increased the percentage of cures. In a few cases nodules have recurred in adjacent areas. These have usually responded to treatment as well as the initial lesion.

Some believe that microscopic study of all nodular lesions should be undertaken to exclude malignant lesions. However, careful review of the literature has shown no cases of malignant degeneration of these myxomatous cystic lesions.

CONCLUSION

Ganglions, synovial cysts and like lesions are a myxomatous degeneration of fibrous tissue cells of the dermis, aponeuroses or other fibrous structures. Histologically they are identical and are produced as the result of minor trauma and friction.

Treatment with roentgen rays with a peak of 150 kilovolts through 3 mm. of aluminum and two doses of 500 r each in one week has produced the most satisfactory results of any known method of treatment. Disadvantages of this treatment are commented on, and it is my belief that in most cases, particularly when symptoms are produced by the lesions, the slight residual atrophic patch is not too great a contraindication to this method.

If some should believe that the residua are a contraindication to the use of this as a primary method, it would still be of importance in the treatment of lesions in the many cases in which there is recurrence after simple excision.

434 Metropolitan Building.

ABSTRACT OF DISCUSSION

DR. HARTHER L. KEIM, Detroit: I should like to congratulate Dr. Woodburne on his convincing presentation, not only on the manner in which he handled this abundant material and the conclusions that he drew but, in particular, his attempt to simplify once again and correlate terminology. Such efforts always appeal to me. While the problem of terminology is here not nearly so urgent as in pachyonychia congenita, as was outlined for us yesterday by Dr. Montgomery, it would seem that if synovial cysts of the fingers, ganglions and some of the epidermal cysts have a common pathologic basis and are myxomatous degeneration cysts, then such a term should be used to cover this particular group of diseases.

Dr. Woodburne has convinced me that these lesions, the so-called myxomatous degeneration cysts, have nothing to do with the synovial system. We will find in both dermatologic and surgical literature a diversity of opinion expressed as to their relationship with the synovial system. Here in this audience are a number of persons who have expressed different opinions on each side of this question.

I think that the fact that these cysts have no endothelial or epithelial lining and that the content is definitely mucoid certainly leaves this group of diseases without any association with the synovial tendon.

With reference to treatment, it has been my experience that up to the present time surgeons are usually best qualified to attempt complete removal. Dr. Woodburne has, however, called attention again to the fact that surgical approach is not always satisfactory. Consequently, I feel that his recommendations with reference to roentgen ray therapy should be borne in mind, especially for patients with small lesions, in whom this rather sizable dose would probably not result in radiation dermatitis.

Dr. H. J. Templeton, Oakland, Calif.: The lesions on the dorsum of the knuckle are old enemies of all of us. We have all treated many of them, I am sure. My own therapeutic results have been poor. I have treated these lesions by simple excision; I have treated them by electrocoagulation followed by curettage and reelectrocoagulation and by destruction with actual cautery, and they have recurred rather uniformly.

I am glad to hear Dr. Woodburne tell about his results from roentgen rays, because possibly I will try it again, but I have given many of these lesions 1,500 roentgens, with a peak of 90 kilovolts, unfiltered, or treated them for three hours with a half-strength 10 mg. radium plaque, with 1 mm. of brass filtration, which is effective in plantar warts, and nothing has happened except an erythematous reaction of the lesion and a persistence or recurrence of the cyst.

My practice now is to tell patients that these lesions are harmless and that they do not have to be treated unless they are sufficiently annoying. If they think that treatment is necessary, I refer them to an orthopedic specialist who does a rather interesting operation. He excises the lesion which is on the dorsum of the knuckle, makes a U-shaped flap on the lateral border of the finger and swings that up, covering the denuded area. His results in the few patients I have referred to him have been good in comparison with mine, which have been poor.

Dr. Richard L. Sutton Jr., Kansas City, Mo.: Dr. Woodburne has made the valuable and practical point that suitable roentgen ray therapy is extremely effective and should be the first choice of therapeutic effort in such cases. I believe that his success depends partly on irradiating a wide enough area, rather than screening down too close to the exact edge of the lesion, for peripheral fibrotic tissue can undergo myxomatous degeneration and so lead to recurrence. Such, perhaps, is the explanation of recurrence after operation.

In electing surgical treatment, one does not hesitate to produce scarring and permanent alteration when these are inescapable. Radiologic therapy may deliberately and unhesitatingly scar, too, given appropriate circumstances. It is interesting that the effective dose is that which necrotizes fibrous tissues and that lesser dosage does not do the job.

Dr. Woodburne and others have shown that these lesions usually possess a dense fibrous capsule. Their structure suggests that they represent cystic degeneration in a fibrotic nodule. Since the fibrotic tissue of the nodule undergoes myxomatous degeneration productive of a substance like synovial fluid, one may surmise that this mesodermal tissue is of synovial nature or potentiality, improperly located.

Savatard, in 1924, illustrated the fibrotic nodule of which I speak. The paper of MacKee and Andrews, of 1922, was the source of Sutton's illustration 539 in the tenth edition of "Diseases of the Skin." This illustration shows clearly the fibrotic capsule within which degeneration has occurred.

But in figure 536 of this text is shown what was clinically a typical synovial lesion; yet a multicellular epithelioid lining was present, and the lesion was interpreted by W. F. Harvey, of the Royal College of Physicians Laboratory in Edinburgh, as synovial endothelioma.

Of some 56 cases of Dr. Woodburne—38 of the wrist, 10 of the hand, 4 of the fingers and 4 of the ankles—the lesions of the fingers apparently are in the minority. I am not sure that all clinically similar so-called synovial lesions of the fingers represent, in fact, the same pathologic process, nor am I certain that ganglions of the wrist and elsewhere are identical with the lesions of the fingers, for synovial sarcoma is not excessively rare as a complication of synoviomas near large joints, while sarcoma from the lesions of the fingers has, so far as I know, never been reported.

Dr. George C. Andrews, New York: I think that we are all in agreement, in the first place, that these lesions result from a myxomatous degeneration of fibrous tissue. Whether that fibrous tissue comes first as a fibroma and then degenerates or whether it does not come that way is a matter which has not been decided.

The point that these lesions usually occur in middle-aged persons, often in persons who have enlargements of the joints due to arthritis, is worth mentioning. As Dr. Sutton says, there may be a connection with the synovial membrane in these lesions, even though they are not definitely proved to be synovial cysts. I have for several years called them periarticular fibromas which have undergone myxomatous degeneration, on the advice of a well known pathologist who has studied the subject.

When these lesions are dissected carefully, one can frequently demonstrate a fibrous cord connecting the lesion with the capsule of the underlying articulation.

I think that one point in Dr. Woodburne's paper which is important for us to remember is that they are usually multiple. It is important to tell the patient of this fact if one is going to give surgical treatment. One may cut out the lesion and another may come.

Another point is that from treatment with injections immobility of the joint may result.

As to treatment with roentgen rays, I have periods in which I am enthusiastic about it and other periods in which I feel as Dr. Templeton does. I think that the dosage which has been most successful, in my experience, is that advised by Dr. Woodburne—fairly high voltage with filtration and fairly large doses, repeated two or three times.

Dr. Fred Wise, New York: I wish that Dr. Woodburne, in closing, would give us a general idea of the response to roentgen ray therapy of the different methods which he described with respect to lesions the size of a pea, let us say, on the index finger and a dollar-sized lesion on the flexor surface of the wrist. It seems to me that there must be a great difference in response in lesions varying in size, and I should like to know whether he changes his technic and his filtration, depending on the size of the lesion.

Dr. George M. MacKee, New York: It is perhaps unfortunate that the method of election for the treatment of these lesions is with roentgen rays, particularly because the dose must be a reactive one. I can detect an element of danger there, which I think Dr. Woodburne also recognizes, because a dose of that quantity, as he states, does leave a defect caused by the irradiation—in other words, chronic radiodermatitis.

In a certain proportion of patients who are young enough to have an expectancy of life of ten or fifteen years epithelioma will develop. Of course, the area is small, which means less danger than would be the case with a larger area.

The plastic surgeons and cancer specialists are busy excising chronic radiodermatitis, with the danger potentiality of about 25 per cent, and also excising carcinomas. Therefore, I think that it is well, when one is dealing with benign lesions, not to call treatment with roentgen rays or radium the method of election unless the curative dose is below the amount that will cause a reaction, because even one site of erythema caused by roentgen rays or radium may have undesirable sequelae ten or fifteen years later.

The value of this article, which is important, is the determination of the pathogenesis and the change in the nomenclature. I wonder if Dr. Woodburne studied the mucous retention cysts in this connection.

Dr. Harold N. Cole, Cleveland: I enjoyed this paper, but I should like to ask Dr. Woodburne why it is that practically all these lesions are seen on the extremities—on the ankles or toes, but more particularly on the fingers. We do find them, of course, along the tendon sheaths on the wrists, so that I am not sure that there may not have been at some time some connection with the sheath.

To mention another point in treatment, a good many years ago we had 1 of these patients, a woman who was dissatisfied with the roentgen ray therapy which we had given her, and I sent her to a surgeon friend. He suggested a simple measure that worked in her case, and we have used it, I should say, in 50 per cent of patients with these lesions on the fingers. All that is necessary is the application of a splint and putting the hand at rest. If they will do this for a month or two, 50 per cent of the lesions will go away. I suggest simply that they use it in the daytime.

Dr. Lloyd W. Ketron, Baltimore: I have also had some favorable results in treating these cysts in a manner similar to that used by Dr. Cole. The lesion was incised, the contents removed and the inside of the wall wiped out with pure phenol. A tight bandage was then applied with adhesive tape and left on for two or three weeks. I should also like to back up Dr. MacKee's warning about the use of such large doses of roentgen rays in such benign lesions. It is likely that there may be serious radiation sequelae.

I should like to ask Dr. Woodburne one question: How can one explain the fact that these synovial cysts fill up so quickly after their contents are removed if they are due to myxomatous degeneration of the fibrous tissues?

Dr. Earl D. Osborne, Buffalo: I should like to call attention to one little trick in the treatment of these lesions. Some years ago, in desperation, in treating a recurrent lesion on a patient's finger, I had to do something for it. It had been operated on a number of times with resultant scarring. I told her to put a piece of adhesive plaster around her finger as tightly as she could, without shutting off the blood supply. I saw her four weeks later, and the lesion was gone.

Since then, I have employed this pressure treatment in a number of cases, and in 40 or 50 per cent of them the lesion disappears, not to return. A minimum of eight weeks should be allowed. Pressure treatment should be used postoperatively, after destruction by electrothermic means.

Dr. Martin T. Van Studdiford, New Orleans: This borders on a little work which my colleagues and I have been doing in treating birthmarks and cysts with rubber pressure bandages. Later on, I want to read a paper on that—I won't tell you too much about it—but we use a rubber sponge, and on 2 or 3

patients with lesions too large for treatment with radium or roentgen rays, we have used rubber pressure bandages. We have cut kneeling pads into pieces of the proper size, left them on for three to five weeks sometimes and had satisfactory results.

Dr. James R. Driver, Cleveland: I should like to emphasize what Dr. MacKee said in regard to irradiation in these cases. Several years ago Dr. Cole and I had a patient with one of these lesions on a finger. We treated it with roentgen rays, as I recall now 1,000 r, unfiltered, and 100 kilovolts through a small window. Erythema developed, and there developed secondary infection which extended into the tendon sheath, and amputation of the finger was necessary.

Dr. George M. MacKee, New York: Apropos of the pressure treatment, the last case of synovial lesion that I saw was under the finger nail. It caused considerable pain because of the pressure. Relief was obtained by using a dental drill through the nail and into the cyst and emptying the cyst, thus relieving the pressure.

The point is that there was pressure, produced by the nail, and the cyst developed anyway, and it recurred after it was emptied.

Dr. Fred D. Weidman, Philadelphia: Dr. Woodburne has touched off a rich discussion this morning which contains several items that collectively bear on the pathologic changes in the disease.

To begin with, the composition of the lymphatic fluid is highly variable in different parts of the body. Admittedly, synovial fluid and the fluid of the tendon sheaths is a modified lymphatic fluid, and the tendon sheaths lie close to these degeneration cysts. This would mean that there are possibilities for seepage, if not actual rupture of a tendon sheath and the escape of the fluid into the tissues nearby. In that event, the fluid in such situations would be of the order of edema, but the special form of edema connoted by its origin in the tendon sheath.

Now, in order that there shall be a special composition of the fluid in the tendon sheaths, there must be some modifying effects on the part of the cells lining these sheaths (a special metabolic function), and perhaps, inasmuch as there is a common embryologic origin for the connective tissue of the sheath lining and the fibrous tissue round about, the cells of the latter have become improperly differentiated in such a way that they modify the composition of the surrounding edematous fluid.

The observation by Dr. Andrews of a fibrous cord extending from the region of the tendon to these nodules is, I think, encouraging to such a thesis: that there are more highly differentiated cells in the neighborhood of the tendon and that when influences arise (continuous trauma, for example) leading to hyperactivity of the extopic tendon sheath cells the fluid produced is not the ordinary watery edematous one, but one which partakes more of the qualities of the fluid in the tendon sheaths. I realize that this is purely hypothesis.

Incidentally, more attention is being paid to diseases of connective tissues. In the past, it was the diseases of parenchymatous tissues that received the most study, but I think that all of us are aware that of late the degenerative diseases are receiving their due. Fibrositis is an example in point. It is incumbent on dermatologists to inquire in the future as to whether there are additional expressions of generalized fibrous degenerative diseases in other parts of the body, such as fibrosing arthritis, disease of the intervertebral disks and lesions of that order.

Dr. Arthur R. Woodburne, Denver: I want to thank you for a generous discussion.

From my experience, I will have to disagree with the point that Dr. Andrews made about the fibrous tissue cord. I was not able to find fibrous tissue cords in the material which was dissected for me by Dr. Denham and some of our surgical friends in the Army. I could find no regular association between joints or synovial sheaths with these nodules. I think that some other observers have recently made that point in the surgical literature.

I agree entirely with Dr. MacKee, and I tried to make my observations conservative and cautioned of the dangers of resulting radiodermatitis. However, in these patients whose disease does not respond to simpler methods and who are having symptoms, I think that probably the roentgen ray therapy is at times justified.

Dr. Wise commented on the change in the amount of the dosage. Of course, in larger lesions, with the dosage that I mentioned, there will be a more decided reaction than there will be in the smaller lesions. However, it was my observation that greater reaction was usually needed to get a satisfactory result.

ACTION OF SOAP ON THE SKIN

IV. Action of a Soap Containing Little or No Lauric or Oleic Acid

C. GUY LANE, M.D.
AND
IRVIN H. BLANK, Ph.D.
BOSTON

IN THE manufacture of soap, fats are chosen which contain either lauric acid or oleic and other unsaturated fatty acids in order that the final soap have satisfactory lathering, cleansing and physical properties. The fatty acid fraction of an average toilet soap usually contains from 11 to 12 per cent lauric acid and 38 to 40 per cent oleic acid and other acids of one double bond.[1] A satisfactory soap may be prepared which has more lauric and less oleic acid, such as coconut oil soap, or one which has less lauric and more oleic acid, such as olive oil soap. Gardiner[2] and Goldman[3] have stated that coconut oil soaps are more irritating to the skin than other soaps, and this is not an uncommon clinical observation. Soaps made from only olive oil have been thought to be relatively nonirritating to the skin. There has been little or no opportunity to observe the action on the skin of a soap containing neither lauric nor oleic acid, since a soap so prepared is relatively insoluble in water and has poor cleansing properties. This paper will present data on the action on the skin of a detergent which contains little or no lauric or oleic acid.

In the first paper of this series[4] the results of patch tests with the single fatty acids were reported. Among those fatty acids present in soap in any appreciable amount, lauric acid elicited the highest percentage of positive reactions to patch tests. Oleic acid elicited only a few positive reactions. During the past five years patch tests with the

From the Department of Dermatology, Harvard Medical School, and the Massachusetts General Hospital.

1. Lane, C. G., and Blank, I. H.: Cutaneous Detergents, J. A. M. A. **118**: 804-817 (March 7) 1942.

2. Gardiner, F.: Soaps and Their Effects on the Skin: An Analytical Research, Edinburgh M. J. **8**:514-520, 1912.

3. Goldman, L.: Patch Tests with Soaps, M. Bull. Univ. Cincinnati **7**:90-92 (Nov.) 1935.

4. Blank, I. H.: Action of Soap on Skin: I. Patch Tests with Fatty Acids, Arch. Dermat. & Syph. **39**:811-816 (May) 1939.

fatty acids on a large series of patients with recurrent vesicular dermatitis of the hands have confirmed these earlier observations.

In the second paper [5] of this series it was shown that fatty acids are more irritating when they are held on an area of skin of which the surface *p*H is increased by the frequent addition of a buffer solution. This is probably the equivalent of converting some of the fatty acid to a soap. At the time that paper was written the hypothesis was stated that while fatty acids of low molecular weight, such as lauric acid, are irritating to the skin at a low *p*H, the acids of high molecular weight, such as stearic acid, would become irritating only if the cutaneous surface with which the fatty acid is in contact were maintained either at a relatively high *p*H or possibly at not so high a *p*H for a longer period of time. The work of other investigators and our own work reported in this paper support this hypothesis.

A patch test with a sodium soap of a fatty acid is somewhat the equivalent of a patch test with a fatty acid at an elevated *p*H, since the soaps are, of course, more alkaline than the fatty acids themselves. Emery and Edwards [6] have shown that among the sodium soaps of the saturated fatty acids, sodium laurate gives the highest percentage of positive reactions to patch tests. They also showed that the sodium soap of oleic acid, an unsaturated acid, elicited more positive reactions to patch tests than the sodium soap of stearic acid, the corresponding C_{18} saturated fatty acid.

The results of comparable patch tests with the sodium soaps of the chemically pure fatty acids on a large series of patients with recurrent vesicular dermatitis of the hands have been observed by us. Our tests were made in the following manner. A piece of white canton flannel, about 4 mm. square, is fastened to the center of a piece of non-moisture-proof cellophane, about 18 mm. square, with a drop of flexible collodion. A series of these squares is then put onto a 4 cm. strip of adhesive tape. The cloth square is then moistened with a drop of distilled water, and with the moistened tip of a wooden applicator a small piece of the dry sodium soap of a single fatty acid is transferred to the moistened cloth. The adhesive strip, which has one square for each substance to which the patient is being tested, is fastened around the arm, only the inner aspect of the arm being used when the strip is not too long. The strip is held in place more securely if a gauze bandage 2 inches (5 cm.) wide is used over it. This remains on the arm for twenty-four hours and the result is read one hour after it is removed.

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5. Blank, I. H.: Action of Soap on Skin: II. Patch Tests with Fatty Acids at Various Hydrogen Ion Concentrations, Arch. Dermat. & Syph. **39**:817-821 (May) 1939.

6. Emery, B. E., and Edwards, L. D.: The Pharmacology of Soaps: II. The Irritant Action of Soaps on Human Skin, J. Am. Pharm. A. (Scient. Ed.), **29**:251-254 (June) 1940.

The table shows the results of a series of patch tests with the sodium soaps on over 300 patients. We have chosen to try to differentiate between mild and definite erythema, since we feel that mild erythema may result from the friction of the cloth square alone and, therefore, should not necessarily be interpreted as a positive reaction to the soap. It is at once evident that among the soaps of the saturated fatty acids, lauric, myristic, palmitic and stearic, the number of significantly positive reactions to patch tests decreases as the molecular weight of the fatty acid increases (lauric to stearic). This cannot be caused by a high p_H of the soaps of low molecular weight, since the p_H of the soap increases with increasing molecular weight of the soap. It is also seen from the table that there are many more positive reactions to patch tests with the soap of unsaturated oleic acid than with the soap of the corresponding saturated stearic acid. Figure 1 shows the results of a series of patch tests with these five soaps (the flexor surface of the forearm has been used in this one test for photographic purposes).

Reactions to Patch Tests with Sodium Soaps

Soap	Negative	Mild Erythema	Definite Erythema	Papule	Vesicle	Total
Sodium laurate	14	58	126	125	20	343
Sodium myristate	40	135	146	6	0	327
Sodium palmitate	145	155	40	1	0	341
Sodium stearate	288	54	2	0	0	344
Sodium oleate	46	108	139	15	0	308

These results confirm the work of Emery and Edwards,[6] who used a different technic for making the patch tests. These results also suggest that even though an olive oil soap (high in sodium oleate) would be less irritating than a coconut oil soap (high in sodium laurate), neither soap would be as nonirritating as one made primarily from sodium palmitate and sodium stearate.

In the second paper [5] of this series, a technic of testing employing a window patch [7] was described for holding a fatty acid in contact with the skin in the presence of buffer solutions of varying p_H. With this same technic, the four saturated fatty acids (lauric, myristic, palmitic and stearic) are held onto the flexor surfaces of the forearms, and the patient is asked to moisten the areas under each patch with a borate-boric acid buffer solution of p_H 9 once an hour during the waking hours of a test period of twenty-four hours. The result of the test is read one hour after removal of the patches. The lauric acid usually elicits an intense erythematous or papular reaction, the myristic acid a less intense erythema, the palmitic acid usually a negative reaction but occasionally a

7. Guild, B. T.: Window Patch Test, Arch. Dermat. & Syph. **39**:807-810 (May) 1939.

mild erythema and the stearic acid almost always a negative reaction. The results of a test of this type are shown in figure 2.

Thus, it is apparent that even though a fatty acid of low molecular weight, such as lauric, may be irritating to the skin at a p_H of 7 or lower, the fatty acids of higher molecular weight (palmitic and stearic) will probably not irritate the skin even at a p_H as high as 9.

As previously stated, a cake of soap made from palmitic and stearic acid (this mixture is commercially called triple-pressed stearic acid) at a p_H of 9 would be an unsatisfactory detergent. It would be hard, would

Fig. 1.—Reactions to patch tests with the sodium soaps of lauric, myristic, palmitic, stearic and oleic acids.

not lather and would clean poorly. If, however, a nonirritating cleansing agent could be added to such a base, a satisfactory detergent might result.

Oleic acid may be sulfated to varying degrees. A series of patch tests with low sulfated oleic acid (9 per cent organic sulfur trioxide) and high sulfated oleic acid (16 per cent organic sulfur trioxide) showed that the higher sulfated material was less irritating to the skin than the low sulfated acid. In a further investigation the low sulfated acid was fractionated into a high sulfated fraction and an unsulfated fraction. Patch tests with these two fractions again showed the high sulfated oleic acid to be nonirritating, while the unsulfated fraction showed many

positive reactions to patch tests. Thus, it seemed apparent that if oleic acid could be sulfated so as to convert it almost entirely to the sulfato-octadecanoic acid it would be nonirritating to the skin and possibly would produce a satisfactory detergent when used in conjunction with palmitic and stearic acids.

Such a detergent has now been produced.[8] It contains primarily palmitic, stearic and the sulfato-octadecanoic acids adjusted to a p_H of 8.5 plus or minus 0.1. It contains no lauric acid and only a small amount of myristic acid (usually less than 5 per cent of the fatty acid fraction). Since the material has received a high sulfation, the amount

Fig. 2.—Reactions to patch tests with lauric, myristic, palmitic and stearic acids in the presence of a buffer solution of p_H 9.

of residual unsulfated oleic acid is negligible. This detergent has been under clinical investigation for the past three years.

Patch tests with a small piece of this detergent on 211 persons elicited 171 negative reactions, 33 reactions of mild erythema, 6 reactions of definite erythema and only 1 papular reaction. The reaction to a patch test with an average toilet soap with this technic is rarely negative; the reaction is usually definite erythema. A patch test with 2 cc. of an 8 per cent solution of this detergent, according to the technic recom-

8. Manufactured under the name "dermolate" by the National Oil Products Co., Harrison, N. J.

mended by Kooyman and Snyder,[9] almost never elicited even the mild erythema or wrinkling of the skin not uncommonly resulting with an average toilet soap in tests with this same method.

Clinical investigation of this detergent has been limited primarily to its use by over 200 patients with recurrent vesicular dermatitis of the hands. A regular soap is usually thought to aggravate this type of dermatitis. These patients have used the detergent as a general cleanser for all personal hygiene. They have been asked to avoid the use of other soaps while using this detergent. Other types of treatment, such as with boric acid soaks and mild ointments, usually accompanied this change in detergents.

In no instance, have we seen an exacerbation of the dermatitis which could be interpreted as an irritation or acquired hypersensitivity to the detergent. Almost all the patients found it a satisfactory cleanser. Some patients reported that this detergent caused more smarting than regular soap, and others reported less smarting. There has been no consistent impression as to whether the use of this detergent seems to leave the skin "drier" or "oilier." Until a more satisfactory method for the objective evaluation of "oiliness" of the skin is developed, we are forced to rely on the patients' impressions for such an evaluation, and these impressions are not always reliable. Clinical investigations of the use of this detergent for various cutaneous diseases are being continued by us and other dermatologists.

SUMMARY

1. Among the sodium soaps of the single fatty acids commonly contained in soaps (lauric, myristic, palmitic, stearic and oleic), only sodium stearate and sodium palmitate elicit a relatively low percentage of significantly positive reactions to patch tests.

2. Stearic acid and palmitic acid usually elicit a negative reaction when held on the skin in the presence of a buffer solution of *p*H 9.

3. Highly sulfated oleic acid (sulfato-octadecanoic acid) usually elicits a negaitve reaction to a patch test.

4. A solid lathering cake detergent made primarily from stearic, palmitic and sulfato-octadecanoic acids and containing little or no lauric or oleic acid has been observed to be nonirritating to the skin both by patch tests and by clinical investigations.

416 Marlborough Street.

9. Kooyman, D. J., and Snyder, F. H.: Tests for Mildness of Soap, Arch. Dermat. & Syph. **46**:846-855 (Dec.) 1942.

POROKERATOSIS

Review and Report of Cases

PHYLLIS E. JONES, M.D.
AND
DUDLEY C. SMITH, M.D.
CHARLOTTESVILLE, VA.

POROKERATOSIS is an unusual chronic progressive keratoatrophoderma, persisting throughout life and characterized by circinate or oval plaques with an annular hyperkeratotic linear elevation at the border, which progresses peripherally leaving a certain amount of atrophy at the center. There is often a dike or slender furrow running along the summit of the border, from which arises a keratotic ridge.[1]

Mibelli, in October 1893, reported 3 cases of a previously undescribed disease which he named porokeratosis after histologic examination, on the ground that the most important anatomic lesion consisted of hyperkeratosis of the sweat duct and sweat pore.[2] One case described by him had been first observed by Majocchi in 1887. The true nature of the disease in this case had not been recognized, and it had been presented as a case of "ichthyosis hystrix." When Mibelli saw the patient he recognized the lesions as exceptional and different from the disease previously recorded. He reported this case along with 2 others, giving a full description of clinical and histologic observations. Three other cases were mentioned, but referred to only briefly.

Mibelli presented his cases as consisting of lesions beginning as minute dry dirty brown warty cone-shaped elevations, less than 1 cm. in diameter, which spread peripherally, leaving a depressed dry callous center. He described the border as having the appearance of a dike, with a shallow central depression at its summit. In 1 instance a lesion reached such a size that the entire forearm and hand were covered. There was a predilection for the hands, face, genitals, legs and feet.

He designated the disease as essentially chronic, beginning in the early years and continuing throughout life. It was unaccompanied with any inflammatory or subjective symptoms. There was mentioned also

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From the Department of Dermatology and Syphilology of the University of Virginia.

1. Becker, W. S., and Obermayer, M. E.: Modern Dermatology and Syphilology, ed. 1, Philadelphia, J. B. Lippincott Company, 1943.

2. Mibelli, cited by Wright.[21]

a hereditary tendency, illustrated by occurrence of 2 of his cases in brother and sister.

From histologic studies made on several of the lesions Mibelli stated that the disease began as acanthosis of the surface epithelium, accompanied with hyperkeratosis. In an advanced stage, the hyperkeratosis stopped and there was an atrophy of the prickle cell layer through pressure of the already formed keratosis. In these places the hair follicles and sebaceous glands were absent. The process affected chiefly the sweat gland pores, which were filled with a horny black layer. The center of the duct projected like a plume. It was by coalescence of a number of these plugs that the ridge was formed. In the cutis there was some dilatation of the vessels of the papillary and subpapillary parts. There was an infiltration of lymphoid cells about the walls of the vessels. In no place was there migration of these cells into the interspinous spaces of the prickle cell layer.

Respighi reported almost simultaneously a group of 7 cases, which in a clinical and pathologic sense were the same as those described by Mibelli. He observed that the nails were secondarily affected and described them as cloudy, brittle and falling off easily. Spots were seen on the palms and soles. The histologic structure in these cases followed closely that in the cases of Mibelli, but more stress was laid on the involvement of the follicles with horny plugs, which penetrated almost to the acini. It was his idea that there was parasitic hyperkeratosis or parakeratosis of the mouths of the tubular and acinous glands.

In 1898 Ducrey and Respighi [3] published a detailed study of 11 cases. They showed that the mucous membrane as well as the skin could be involved. All parts of the buccal mucous membrane could be affected, and lesions could be recognized even if cutaneous lesions were absent.

Hutchins,[4] of Atlanta, Ga., was the first to report a case of porokeratosis in America, in 1896. His patient had been under observation since 1892, and he recognized the disease as porokeratosis as described by Mibelli after reading his report. The disease began in his patient at the age of 2 years as a seed-wart-like growth just inside the border of the left palm at the radial side of the base of the index

3. Ducrey, A., and Respighi, E.: The Localization on the Buccal Mucous Membranes of the Affection Improperly Called Porokeratosis: Preliminary Note, Ann. de dermat. et syph. **9**:1, 1898; abstracted, J. Cutan. & Genito-Urin. Dis. **16**:545, 1898; Hyperkeratosis Figurata Centrifuga Atrophicans, Improperly Called Porokeratosis: A Peculiar Skin Affection with Localization upon the Skin and Mucous Membrane; a New Clinical and Histological Study, Ann. de dermat. et syph. **9**:609 and 734, 1898; abstracted, J. Cutan. & Genito-Urin. Dis. **16**:546, 1898.

4. Hutchins, M. B.: A Case of Porokeratosis Mibelli, J. Cutan. & Genito-Urin. Dis. **14**:373, 1896.

finger and spread peripherally. In 1896, when the patient was 32 years old, he had lesions on the left palm, the back of the hand, the forearm and the face.

Although Hutchins was the first to report a case in this country, Stelwagon [5] in his treatise on dermatology told of a case seen by him in 1887, the true nature of which he did not recognize until some years later.

The second report to be published in this country was that of Gilchrist [6] in 1897. He reported 11 cases in which it was thought that the disease had followed a course of transmission from grandmother

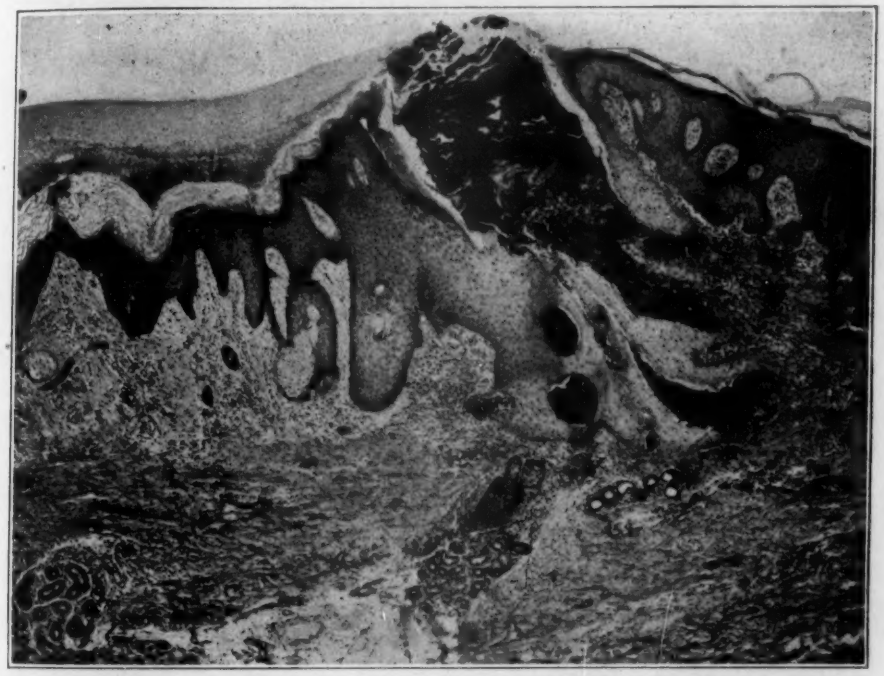

Fig. 1.—Typical follicular plugging, moderate hyperkeratosis and acanthosis. Perivascular infiltration in the corium, with newly formed connective tissue in the papillae.

to grandchildren. In 1899 Gilchrist wrote a complete clinical and histologic description of the 11 cases which he had briefly reported in 1897.

5. Stelwagon, H. W.: A Treatise on Diseases of the Skin, ed. 9, Philadelphia, W. B. Saunders Company, 1923.

6. Gilchrist, T. C.: Eleven Cases of Porokeratosis (Mibelli) in One Family, J. Cutan. & Genito-Urin. Dis. **17**:149, 1899; A Case of Porokeratosis (Mibelli) or Hyperkeratosis Excentrica (Respighi) with a Remarkable Family History, Bull. Johns Hopkins Hosp. **8**:107, 1897.

In June 1897 Joseph [7] gave an exhaustive account of 2 cases which he had encountered in Germany. The following year, 1898, Wende [8] reported the next case occurring in America. Efforts to determine a possible infectious origin of this disease were unsuccessful.

A case reported by Basch [9] in 1898 presented characteristic lesions. After histologic study of these lesions the author agreed that the disease originated in the sweat glands and especially in their epidermal portion. Bacteriologic examinations in this case revealed nothing of significance.

Mibelli in 1899 reported another case in which lesions were observed on the glans penis and in the mouth in a patient 68 years old. The disease was of thirty years' duration and occupied the trunk and both extremities. It was traceable through four generations.

Between 1900 and 1905 there was little reported in the literature concerning porokeratosis. In 1905 Mibelli reported 2 new cases. Truffi [10] in 1905 presented a case in a boy of 13, in whom the lesions had been present since 11 months of age. In 1907 Himmel and Brocq and Pautier [11] reported cases, and in 1908 Baum [12] saw a patient with lesions distributed along the nerve trunk. Isaac [13] presented a case in 1913 in which only the scrotum was involved. Maki [14] reported in 1914 3 cases of porokeratosis. Sellei [15] in 1914 reported a case in a man who had lesions on the palms and soles. In 1916 Matsumoto [16] described a single case, and in 1918 he made a detailed report of 13 cases. MacCormac and Pellier [17] reported a case in 1918. Other cases were reported by Sevenig in 1918, Harris [18] in 1919 and Bruck and Hirsch [19] and Bukovsky [20] in 1920. An excellent review of the literature with

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7. Joseph, M.: Ueber Porokeratosis, Arch. f. Dermat. u. Syph. **39**:334, 1897.

8. Wende, G. W.: Porokeratosis with Report of a Case, J. Cutan. & Genito-Urin. Dis. **16**:505, 1898.

9. Basch, E.: A Case of Porokeratosis (Mibelli), Pest. med.-chir. presse **34**:625, 1898; abstracted, J. Cutan. & Genito-Urin. Dis. **16**:547, 1898.

10. Truffi, M.: Sur un cas de porokératose systématisée, Ann. de dermat. et syph. **6**:521, 1905.

11. Himmel, cited by Wright,[21] and Brocq and Pautier, cited by Wright.[21]

12. Baum, cited by Wright.[21]

13. Isaac, cited by Wright.[21]

14 Maki, G.: Three Interesting Cases of Porokeratosis and Its Treatment, Jap. Ztschr. f. Dermat. u. Urol. **14**:223, 1941; abstracted, J. Cutan. Dis. **32**:530, 1914.

15. Sellei, cited by Wright.[21]

16. Matsumoto, S. I.: A Peculiar Form of Porokeratosis, J. Cutan. Dis. **34**:489, 1916; The So-Called Porokeratosis (Mibelli) with Special Reference to Its Histopathology, ibid. **36**:379, 1918.

17. MacCormac, H., and Pellier, C. de C.: A Case of Porokeratosis, Brit. J. Dermat. **30**:197, 1918.

18. Harris, A.: Porokeratosis, J. Cutan. Dis. **37**:56, 1919.

19. Bruck, W., and Hirsch, H.: Ueber Porokeratosis, Dermat. Ztschr. **29**:223, 1920; abstracted, Arch. Dermat. & Syph. **2**:393 (Sept.) 1920.

20. Bukovsky, J.: Hyperkeratosis Eccentrica, Česká dermat. **2**:61, 1920; abstracted, Arch. Dermat. & Syph. **4**:246 (Aug.) 1921.

the report of a case was made by Wright [21] in 1921. A case occurring in a 16 month old baby was reported in 1921 by Scholl.[22] Foerster [23] and Milian and Lefèvre [24] reported cases in 1922.

This disease, considered rare in France, was reported by Louste, Thibaut and G. Barbier [25] in 1923. Other cases were presented in 1923 by Wile,[26] Finnerud,[27] Gregor [28] and Fulde,[29] by Hodara and Behdjet [30] in 1924 and by Acton [31] in 1927.

Hall [32] described the occurrence of 6 cases of porokeratosis in Chinese patients. Lain [33] in 1928 presented 3 cases in one family. Lewin [34] and Ichteiman [35] reported cases in 1931. A complete review of the literature with an extensive bibliography was published by Moncorps [36] in 1931.

Ritchie and Becker [37] inoculated animals with tissue taken from their patient in an effort to prove an infectious origin. Several typical cases

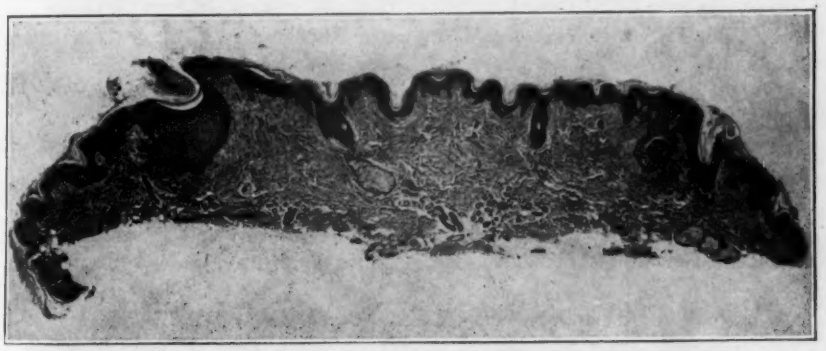

Fig. 2.—Cross section of small lesion, showing acanthosis with follicular plugging at either end of the section and moderate inflammatory infiltration of corium. Sweat glands are present and normal in appearance.

21. Wright, C. S.: Porokeratosis: Report of a Case, Arch. Dermat. & Syph. **4**:469 (Oct.) 1921.

22. Scholl, O. K.: A Case of Porokeratosis Limited to One Side of the Body, Dermat. Wchnschr. **72**:1, 1921; abstracted, Arch. Dermat. & Syph. **4**:394 (Sept.) 1921.

23. Foerster, O. H.: Porokeratosis (Mibelli), Arch. Dermat. & Syph. **5**:796 (June) 1922.

24. Milian and Lefèvre: Porokeratosis of Mibelli, Bull. Soc. franç. de dermat. et syph. **29**:41, 1922; abstracted, Arch. Dermat. & Syph. **6**:206 (Aug.) 1922.

25. Louste, Thibaut and Barbier, G.: Porokeratosis of Mibelli, Bull. Soc. franç. de dermat. et syph. **30**:252, 1923; abstracted, Arch. Dermat. & Syph. **8**:716 (Nov.) 1923.

26. Wile, J.: Porokeratosis, Arch. Dermat. & Syph. **8**:869 (Dec.) 1923.

27. Finnerud, F.: Porokeratosis, Arch. Dermat. & Syph. **7**:708 (May) 1923.

28. Gregor, F. W.: Porokeratosis, Indiana M. A. J. **16**:274, 1923.

29. Fulde, E.: Studien über Vererbung von Hautkrankheiten: IV. Porokeratosis Mibelli, Arch. f. Dermat. u. Syph. **114**:6, 1923.

(Footnotes continued on next page)

were described from 1932 to 1934 by Thompson,[38] Verrotti,[39] Kobayasi [40] and Kauczynski.[41] Ambler and Stout [42] in 1934 presented a case of porokeratosis occurring in a Negro. Only 2 other instances had been mentioned previously in which this disease was recognized in Negroes, 1 by Hutchins [4] and the other by Tauber [43] in his discussion of the case reported by Ambler. Reports of cases were published by Shiller,[44] Gross,[45] and Andrews [46] in 1937.

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30. Hodara, M., and Behdjet, H.: Histologic Investigation of a Case of Porokeratosis of Mibelli, Dermat. Wchnschr. **77**:1168, 1923; abstracted, Arch. Dermat. & Syph. **9**:760 (June) 1924; A Second Case of Porokeratosis of Mibelli, Dermat. Wchnschr. **77**:1167, 1923; abstracted, Arch. Dermat. & Syph. **8**:760 (June) 1924.

31. Acton, H. W.: Porokeratosis: Its Causation and Treatment, Indian J. M. Research **15**:349, 1927.

32. Hall, G. A. M.: Porokeratosis (Mibelli): Report of Its Occurrence in Six Chinese Patients, Arch. Dermat. & Syph. **18**:396 (Sept.) 1928.

33. Lain, E. S.: Porokeratosis: Report of Three Cases, Urol. & Cutan. Rev. **32**:383, 1928.

34. Lewin, L.: A Case of Porokeratosis Mibelli, Sovet. vestnik dermat. **9**:176, 1931; abstracted, Arch. Dermat. & Syph. **24**:1091 (Dec.) 1931.

35. Ichteiman, M. S.: Clinical and Histologic Study of Porokeratosis Mibelli, Sovet. vestnik dermat. **9**:674, 1931; abstracted, Arch. Dermat. & Syph. **26**:517 (Sept.) 1932.

36. Moncorps, C.: Porokeratosis Mibelli, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankeiten, Berlin, Julius Springer, 1931, vol. 8, pt. 2, pp. 463-481.

37. Ritchie, E. B., and Becker, W. E.: Porokeratosis (Mibelli): Report of a Case; Histologic Study and Animal Inoculation, Arch. Dermat. & Syph. **26**:1032 (Dec.) 1932.

38. Thompson, M. S.: A Case of Porokeratosis of Mibelli, Brit. J. Dermat. **44**:544, 1932.

39. Verrotti, G.: A Peculiar Case of Porokeratosis Mibelli with Corneomas, Gior. ital. di dermat. **74**:3, 1933; abstracted, Arch. Dermat. & Syph. **28**:572 (Oct.) 1933.

40. Kobayasi, T.: Generalized Porokeratosis Mibelli with Lesions of the Buccal Mucosa and of the Nails, Jap. J. Dermat. & Urol. **36**:439, 1934; abstracted, Arch. Dermat. & Syph. **31**:715 (May) 1935.

41. Kauczynski, K.: Porokeratosis Mibelli, Przegl. dermat. **29**:294, 1934; abstracted, Arch. Dermat. & Syph. **32**:115 (July) 1935.

42. Ambler, J. V., and Stout, K. L.: Porokeratosis (Mibelli): A Report of Its Occurrence in a Negro, Arch. Dermat. & Syph. **29**:20 (Jan.) 1934.

43. Tauber, E. B., in discussion on Ambler, J. V.: Porokeratosis Mibelli, Arch. Dermat. & Syph. **25**:1158 (June) 1932.

44. Shiller, A. E.: Porokeratosis of Nevoid Type, Arch. Dermat. & Syph. **35**:1187 (June) 1937.

45. Gross, P., and Barker, L. P.: A Case for Diagnosis (Porokeratosis Mibelli), Arch. Dermat. & Syph. **36**:179 (July) 1937.

46. Andrews, G. C.: Porokeratosis (Mibelli), Disseminated and Superficial Type, Arch. Dermat. & Syph. **36**:1111 (Nov.) 1937.

Scholtz,[47] Ayres and Anderson[48] in 1939, Johnson[49] in 1941, Rosen[50] in 1942; and Bloom and Abramowitz[51] and Franks and Davis[51a] in 1943 reported cases.

There has been a great diversity of opinion throughout the literature as to the classification of porokeratosis. It has been generally classified either with the verrucae or the nevi. In favor of the former is the wart-like appearance of the lesions, particularly in the early stages, the histologic picture of hypertrophy of the epidermis and the papillae and the decided hyperkeratosis. The familial tendency, the persistence of the lesions throughout life, the noncontagiousness, the occasional systematic arrangement and the failure to respond to roentgen rays all favor the placing of porokeratosis in the classification of the nevi.

Numerous theories have been proposed by many investigators as to the cause of porokeratosis, but it must still be regarded as a disease of unknown origin. It cannot be denied that heredity plays a part. Cockayne[52] has shown that the method of inheritance is one of regular dominance, since transmission is invariably direct and there is no instance of an apparently normal person's acting as a transmitter. Taking all cases together the proportion of affected males to affected females is 164 to 69, a ratio of more than 2 to 1. Mibelli finally came to the conclusion that porokeratosis could be included with the nevoid dermatoses of a definitely hereditary and familial type and might be described as keratoatrophic nevus. In Truffi's[10] case and a few others the distribution would suggest probably a neurogenous origin, since each group of lesions was mapped out according to the distribution of a peripheral nerve. Attempts to produce an organism or a parasite have failed. No lesions have ever appeared at the site of injection except in Wende's one successful inoculation of his original patient and in the case of Ritchie and Becker, when in one instance they obtained similar microscopic changes in the skin of a guinea pig following the injection of macerated material obtained from a patient with porokeratosis. There

47. Scholtz, J. R.: Porokeratosis (Mibelli), Arch. Dermat. & Syph. **39**:574 (March) 1939.

48. Ayres, S., and Anderson, N. P.: Porokeratosis (Mibelli), Arch. Dermat. & Syph. **39**:574 (March) 1939.

49. Johnson, H. H.: Porokeratosis (Mibelli), Arch. Dermat. & Syph. **43**:574 (March) 1941.

50. Rosen, I.: Porokeratosis Mibelli, Arch. Dermat. & Syph. **45**:782 (April); 982 (May) 1942.

51. Bloom, D., and Abramowitz, E. W.: Porokeratosis Mibelli: Report of Three Cases in One Family, Arch. Dermat. & Syph. **47**:1 (Jan.) 1943.

51a. Franks, A. G., and Davis, M. I. J.: Porokeratosis (Mibelli) Associated with Cutaneous Horn, Dystrophy of Nails and Atrophy of Interosseous Muscles: Report of a Case, Arch. Dermat. & Syph. **48**:50 (July) 1943.

52. Cockayne, E. A.: Inherited Abnormalities of the Skin and Its Appendages, London, Oxford Medical Publications, 1933.

is nothing to recommend a theory of contagion for this disease and much against it. In no case has the wife or the husband of a patient having porokeratosis been affected with the disease. All attempts with inoculation and all attempts to grow an organism on various mediums have been without results; and special stains have shown nothing. Ichteiman [35] expressed the belief that the disease could not be considered nevoid in character and that it belonged to the group of dyskeratoses of Darier. Acton [31] stated the belief that the disease was merely a type of localized hyperkeratosis, with central atrophy and associated with hypofunction of the thyroid gland. He reported complete cures in 3 cases with thyroid therapy.

It has been recognized for a number of years that vitamin A deficiency produces cutaneous abnormalities, characterized by a follicular keratosis or dyskeratosis. The skin with a typical cutaneous eruption from vitamin A deficiency is described as dry and rough, with localized follicular papules containing a central intrafollicular keratotic plug. The plugs frequently project from hair follicles as horny spines. The sweat apparatus is said to be involved in this disease, but to a less extent than the hair follicles and sebaceous glands. The lesions may be generalized or localized, but are usually symmetrically distributed. Some of the first studies on the cutaneous manifestations of vitamin A deficiency were carried out by Frazier and Hu.[53] The principal microscopic observations, as shown by these investigators in their cases of proved vitamin A deficiency, revealed that the pathologic process was primarily hyperkeratinization of the lining epithelium of the hair follicles. Keratosis follicularis has been reported as improved with treatment with vitamin A and has some clinical and microscopic characteristics resembling porokeratosis.

We can demonstrate now that there are certain clinical and histologic characteristics of porokeratosis and vitamin A deficiency which are closely related and suggestive of a common cause. The most consistent cutaneous lesion in these two diseases is a keratotic papule or groups of papules. In porokeratosis the earliest lesion is a single papule with a keratotic surface. In vitamin A deficiency a group of keratotic papules appear either localized or generalized, and they are accompanied with a dry skin and a reduction or absence of sweating. The lesions are usually symmetrically arranged in both diseases.

Histologically these diseases resemble each other in that there is a plugging of the hair follicles and sweat ducts, with a dense mass of cornified cells and hyperkeratosis involving these areas and to a less extent the surrounding tissue. In porokeratosis there is a cellular infiltration of the corium beneath the hyperkeratotic area. In vitamin A

53. Frazier, C. N., and Hu, C. K.: Nature and Distribution According to Age of Cutaneous Manifestations of Vitamin A Deficiency, Arch. Dermat. & Syph. 33:825 (May) 1936.

deficiency there is a moderate lymphocytic infiltration in the area where the sebaceous glands have been damaged or have atrophied. There is also homogenization and sclerosis of the connective tissue. In porokeratosis, beneath the atrophic area the collagen becomes sclerotic and the hair follicles and sebaceous glands and at times the sweat glands disappear.

From the foregoing, we propose the theory of vitamin A deficiency as a causative factor in porokeratosis. We have neither proved nor disproved this theory, but merely present it as a possibility. We have been unable to follow the cases reported in this paper since the idea of vitamin A deficiency was considered and have therefore had no opportunity for putting it to trial.

Mibelli classified this disease as one of the incurable dermatoses. Many and varied treatments have been tried, mostly without success. Total excision or destruction of the lesions by electrocautery has given the best results. There have been reports of recurrence of the lesions at the site of destruction with electrodesiccation or cauterization, but this is the treatment of choice in early stages of the disease. The use of solid carbon dioxide has generally proved unsatisfactory. Roentgen and radium therapy have been unsuccessful. Local treatment with mercury ointments and various keratolytic agents has been valueless. Potassium iodide and compounds of mercury and other heavy metals have been given by mouth without effect. Curettement followed by cauterization of the base of the lesion with silver nitrate or other caustics has been used by many, but frequently results in recurrence of the lesion within a few months.

Acton [31] observed that a high percentage of his patients had a low basal metabolic rate. He treated these patients with a large dose of thyroid extract and reported immediate improvement with cures in two weeks. His work, however, has not been substantiated by other investigators.

REPORTS OF CASES

CASE 1.—G. T., an 18 year old white youth who had congenital syphilis with juvenile paresis, was first brought to the University of Virginia Hospital in 1941 when he began to show evidence of mental deterioration. On routine examination the boy was observed to have unusual keratotic lesions on the back of the neck and the right arm. He also had blue scleras and a history of numerous fractures of the legs and arms, and from this a diagnosis of fragilitas ossium was made.

This boy first experienced cutaneous lesions on his neck at the age of 12. The only symptom was slight itching. The lesions on the neck slowly increased in size, and new ones appeared on the right arm, beginning as tiny red papules and extending peripherally in ring formation. No treatment had been tried except for "sulfur and lard" as a home remedy.

The patient was born out of wedlock of a syphilitic mother. There was no history of similar cutaneous lesions in the mother or maternal grandparents. It is not known whether the father or any of his family were affected.

Physical examination revealed a poorly developed, abnormally small and mentally retarded boy who appeared about 10 years of age. There was a moderately severe acne of the face, back and shoulders. There were a few keratotic cutaneous lesions on the neck and forearms. The sclerae were blue.

In November 1944 this patient was observed to have eight peculiar cutaneous lesions of various sizes on the neck and both forearms. On the right side of the back of the neck there was a large gyrate lesion about 0.75 by 1.25 inches (about 1.9 by 3.2 cm.) in diameter.

Three lesions were present on the left forearm. These were annular lesions 1 by 0.75 inch (2.5 by 1.9 cm.), 1 by 0.5 inch (2.5 by 1.27 cm.) and 0.5 by 0.5 inch (1.27 by 1.27 cm.) in diameter, respectively. They appeared on the flexor surface, slightly distal to the cubital area and were grouped close together. These lesions also presented a depressed slightly atrophic central area, with a raised hyperkeratotic border composed of closely adherent papules, as described for the other areas. One of the smaller lesions was excised for microscopic examination, and a small keloid developed in this area. On the right forearm were three small

Fig. 3.—Porokeratosis (case 1).

lesions, which had developed in the past year. These lesions consisted of small individual papules with dark rough keratotic tops.

Numerous routine and special laboratory tests were made, without any significant observations. Wassermann and Kahn reactions of the blood were strongly positive. Examination of the spinal fluid showed grade I changes for neurosyphilis.

All the cutaneous lesions originated as single papules, but soon a group of three or four new papules appeared. The lesions spread peripherally, forming an annular plaque with a typical border or keratotic ridge. The center of each lesion became depressed below the surface of the ridge and appeared atrophic. Growth of all these lesions was slow but progressive.

No treatment of the cutaneous lesions was attempted. There has been no recurrence of the lesion that was excised for microscopic examination. The patient received regular antisyphilitic treatment with arsenic and bismuth compounds and fever induced with typhoid vaccine, with no effect on the skin.

The section of skin from the neck was shown by microscopic examination to consist of a rather thick hyperkeratotic plaque, located at a sweat gland opening.

The plugged pore was filled with desquamated squamous cells and a large number of polymorphonuclear leukocytes. The pore could be traced to a sweat gland, and the stratified squamous epithelium in the walls of the pore was greatly thickened because of an increase in the keratinization of the cells. The sweat glands beneath the lesion were distended. The corium in the region of the plaque showed perivascular infiltration with lymphocytes and a few polymorphonuclear leukocytes. There appeared to be considerable newly formed connective tissue in the papillae and also some fibrous proliferation about the sweat glands. Other than slight hyperkeratosis no conspicuous changes were seen in the epidermis adjacent to the plaque.

A second biopsy specimen was taken from a small young lesion on the arm. Microscopic examination of this section revealed a definite localized type of acanthosis with mild hyperkeratosis and a thick stratum granulosum, located so as to involve both sweat pores and follicles. A deep intraepidermal dilated area occurred at one point and was filled with horny material and leukocytes. The sweat glands were numerous. Their ducts were studied by serial sections, but no great changes were evident until the epidermis was reached. In most areas the duct throughout

Fig. 4.—Porokeratosis (case 2).

its progress was normal. Immediately surrounding the epithelium of a dilated pore were macrophages, a few lymphocytes and a few foreign body giant cells. A light inflammatory infiltrate was present in the corium. There was some vascular and connective tissue proliferation in the papillae.

Case 2.—A white schoolboy, 16 years of age, was seen on Sept. 2, 1943, for treatment of acne of the face and back. During the routine examination two unusual hyperkeratotic lesions were noted on each side of the back of the neck. These lesions had been present three or four years and had produced no symptoms. His local physician had cauterized one area previously, effecting a decrease in its size, but the lesion was still present.

Examination revealed an irregular circinate area about 3 cm. in diameter on the right side of the back of the neck, with a similar but smaller lesion about 2 cm. in diameter, slightly anterior to and below this. On the left side of the neck there was a large semicircular plaque about 3 cm. in diameter, with a smaller annular lesion about 0.75 cm. in diameter and posterior to the larger lesion. The central portion of each lesion showed atrophy of the skin. Surrounding the central atrophic

area was a hyperkeratotic ridge. This was composed of closely arranged tiny conical elevations, some of which had fused to form the ridge. It was reddish brown and had a hard rough surface, forming an incomplete seam on top of the ridge.

The patient refused a biopsy, and no laboratory studies were obtained. He did not return for further examination or treatment.

SUMMARY

Porokeratosis is an unusual chronic and progressive cutaneous disease which persists throughout life and is characterized by circinate or oval plaques composed of a hyperkeratotic linear border which progresses peripherally leaving some atrophy at the center. There is a slender furrow running along the center of the peripheral wall from which arises a keratotic ridge.

This disease was first recognized and described by Mibelli in 1893. Since then it has been reported by authors from many countries, including the United States.

The cause remains debatable. That there is a definite hereditary factor has been shown repeatedly by reports of several cases of porokeratosis occurring in one family. Cockayne has shown that the method of inheritance is one of regular dominance, since transmission is invariably direct. Parasitic and infectious origin has been fairly well ruled out by bacteriologic studies and inoculation of animals. The theory that this is a nevoid condition has been favored by many. Hypofunction of the thyroid gland has been suggested as a cause, but has not been substantiated by other investigators. We are, in this paper, suggesting another possible causative factor, which has not been discussed previously. The clinical and histologic observations indicate a possible relationship between porokeratosis and vitamin A deficiency. A brief description of these diseases, pointing out both clinical and histologic similarities, is presented. No investigations have been made to prove this theory, but we offer it as a basis for future study. Until more is known about the physiologic and chemical nature of this disease one should continue to consider it a disease of unknown origin.

Onset of the disease is commonly in childhood, but it may occur any time during adolescence or early adult life. It affects males three times as frequently as females. Porokeratosis should be classed with the incurable dermatoses, since treatment has been unsatisfactory in the majority of cases. Total excision of the lesion is the most reliable means of eliminating the disease but this is suitable only when lesions are small and few.

Two cases of porokeratosis are presented, both occurring in adolescent boys and beginning at about the age of 12, with slow progression of the lesions. In both cases lesions were presented which were clinically typical of the disease. Microscopic sections from 1 of our patients showed characteristic histologic observations of porokeratosis.

LICHEN PLANUS IN THE NEGRO

L. H. WINER, M.D.
AND
H. LEVITT, M.D.
BEVERLY HILLS, CALIF.

LICHEN planus in the Negro offers a challenge in its clinical diagnosis and interesting histologic characteristics in microscopic examination. Cutaneous eruptions in the Negro have often been clinically masked by the intensive content of melanin. Further, the pigmentation of eruptions in the Negro has often been increased and at other times diminished. Frequently lichen planus has been known to have been followed by vitiligo.

SUMMARY OF LITERATURE

Fox,[1] in 1910, presented a case of lichen planus in a Negro woman, which early showed large numbers of typical lichen planus papules, but later the typical eruption was replaced by increased pigmentation.

Jacob,[2] in a study of 179 cases of lichen planus in St. Louis, observed only 5 cases in Negroes and stated that Gilchrist, at Johns Hopkins Dispensary in Baltimore, saw only a half-dozen cases in twenty years. He stated that the eruption was typical in every respect except in color. In this respect the dark-skinned persons showed grayish papules.

Jacobson [3] presented a case in a 24 year old Negro man, in which the lesions had become confluent and formed circinate dark brown plaques with smooth depressed centers and elevated ridges, the latter being the color of the patient's normal skin. Frank [4] presented a case of lichen planus in a 5½ year old Negro boy, with a generalized symmetric eruption consisting of violaceous papules.

Hollander and Baer [5] reported a Negro boy aged 12 for whom a diagnosis of lichen planus annularis hypertrophicus had been made.

From the Division of Dermatology, University of Southern California, Los Angeles, and Los Angeles County General Hospital.

1. Fox, H.: Lichen Planus in a Negress, J. Cutan. Dis. **28**:403 (Aug.) 1910.
2. Jacob, F. M.: Some Studies on Lichen Planus, Based on the Study of One Hundred and Seventy-Nine Cases, Arch. Dermat. & Syph. **2**:607-616 (Nov.) 1920.
3. Jacobson: Lichen Planus, Arch. Dermat. & Syph. **3**:848 (June) 1921.
4. Frank: Lichen Planus in a Colored Child, Arch. Dermat. & Syph. **20**:114 (July) 1929.
5. Hollander, and Baer: Lichen Planus Annularis Hypertrophicus, Arch. Dermat. & Syph. **17**:439-40 (March) 1928.

In this patient pigmentary changes were evidenced by an especially black center in all the lesions. The lesions on the arms had a lichen shine.

Juliusberg [6] mentioned that lichen planus in the Negro races is rare and that in some cases the papules are darker than the normal skin while in others they vary from a violet hue to gray in dark Negroes.

Appel [7] presented a case in a 40 year old Negro man and stated that he had seen a second case in a Negro woman and speculated that the incidence in Negroes is not so rare as was heretofore believed.

CLINICAL APPEARANCE AND CHARACTERISTICS

The clinical appearance of lichen planus in Negroes has many interesting features which are more manifest than those of lichen planus in white persons.

The color, instead of being violaceous red, varies from purplish gray to black. The early lesions are lighter in color and elevated. The late lesions are hyperpigmented. The waxy sheen which is evident early is lost in the late lesions.

The polygonal border of the individual papules is not as acute as in white persons.

HISTOLOGY

The microscopic picture of lichen planus in the Negro has rarely been reported.

Early in the disease, hyperkeratosis, increased granulosis and formation of lacunae are present. The pigment normally seen in the numerous layers of the epidermis of Negroes has disappeared. This is especially noticeable in the stratum basale, which is involved by intense colliquative degeneration and is so intense in some areas that small vesicles are formed at the junction of the epidermis and cutis.

Invasion of the epidermis by lymphocytic and polymorphonuclear cells is especially evident at the lower border of the epidermis.

There is a dense cellular infiltration in the papillary cutis, consisting of lymphocytes, polymorphonuclear neutrophils and numerous chromatophores densely packed with pigment.

In late stages the microscopic section shows increased pigmentation in the epidermis, which in early stages was washed out. Atrophy of epidermis is present, recurrence of pigment of the basal layer is observed and heavily pigmented chromatophores persist in the cutis.

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6. Juliusberg, F., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 7, pt. 2, p. 27.

7. Appel, B.: Lichen Planus Hypertrophicus, Arch. Dermat. & Syph. **53**:187 (Feb.) 1946.

Fig. 1.—Early lichen planus lesion in a Negro, showing discoloration.

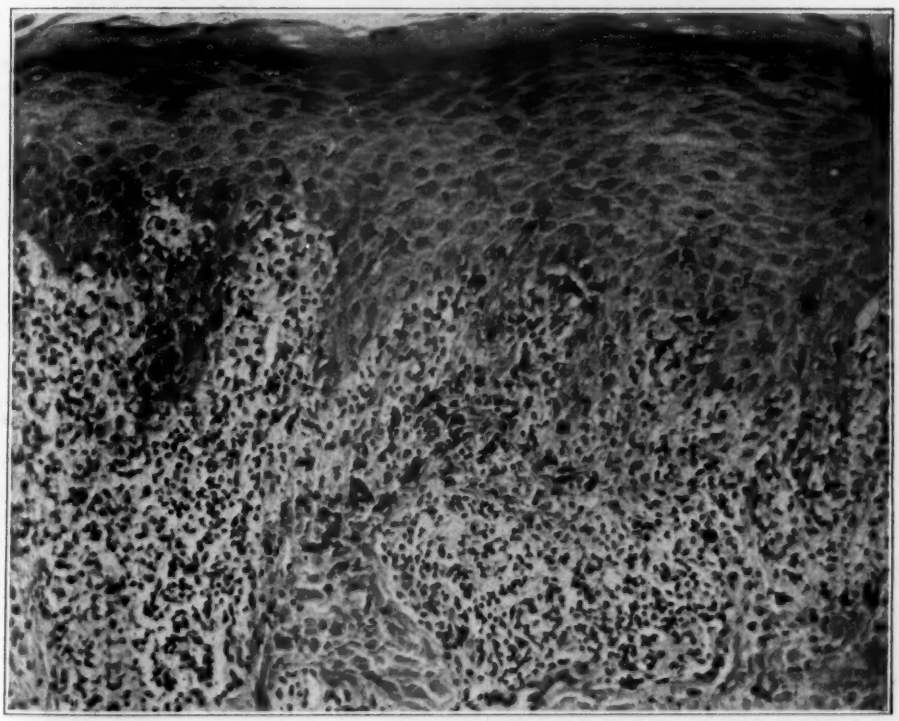

Fig. 2.—Histologic section of a lesion of early lichen planus in a Negro, showing intense granulosis, loss of pigment from basal cells and dense nests of chromatophores in the cutis.

REPORT OF CASES

CASE 1.—O. L., a 44 year old Negro woman, had a subtotal hysterectomy and appendectomy in July 1945, and at this time she noticed the appearance of "whitish spots" on the inner aspect of her left thigh. These lesions became enlarged and assumed a darker hue. Two to three months later she noticed similar lesions about her abdominal scar and also became aware of lesions in her mouth. The lesions of her thigh and abdominal scar were pruritic.

Fig. 3.—Late lichen planus in a Negro, showing hyperpigmentation and absence of discrete borders of papules.

In March 1946 the lesions consisted of 0.5 to 1.5 cm. flat-topped plaques, extending over an area of 3 by 12 cm. on the inner side of the left thigh. There were also a few 0.5 cm. papules about the lower edge of her recent abdominal scar. The lesions were dark brown, irregularly shaped and somewhat shiny. There were reticular whitish plaques, 1 cm. in size, on the mucous membrane of both cheeks.

CASE 2.—L. B., a 49 year old Negro woman, first noticed a reddish papule, 3 mm. in size, on the inner aspect of her left thigh five years before she consulted us.

The lesion gradually increased in size, turned darker and developed satellite lesions which were similar to the original lesion.

Examination in March 1946 revealed a shiny hyperthrophic plaque, 1 by 3.5 cm. in size, on the inner aspect of the left thigh, which was lighter than the heavily pigmented surrounding skin. There were several adjacent papules of pinhead size. No oral lesions were present.

Fig. 4.—Histologic section of a late lesion of lichen planus, showing atrophy of epidermis, recurrence of pigment in the basal cells and dense collections of chromatophores in the cutis.

CASE 3.—R. J. B., a 54 year old Negro, first noticed lesions on his right hip four to five months before we saw him.[8] Lesions then developed on the penis, scrotum, wrists, upper part of the chest and legs. The lesions were nonpruritic.

In May 1946 there was a smooth irregular hyperpigmented plaque, 2 by 4 cm. in size, on the right thigh, which was hyperkeratotic at one edge. On the glans

8. Dr. H. M. Elliot enabled us to study and report this case.

penis there were ring forms, and on the shaft of the penis and on the scrotum were depigmented grayish hyperkeratotic patches, consisting of small papules. The annular plaque on the glans consisted of discrete papules. On the flexor surfaces of the arms were plaques, 1 cm. in size, with depressed hyperpigmented centers and raised lichenified edges. There were hyperpigmented brown spots of healed lesions and also elevated split-pea size bluish new lesions on his chest.

COMMENT

We have presented 3 cases of lichen planus occurring in Negroes. The clinical characteristics of depigmentation early in the disease and hyperpigmentation late in the disease are explained by the histologic observations. The grayish lesions are explained by the intense hyperkeratosis, granulosis and loss of pigment from the epidermis. The late black lesions are explained by the recurrence of pigment in the epidermis, the persistence of pigment in the cutis and an atrophy of the epidermis. This disease is not frequently observed in Negroes. Only 17 cases have been previously reported in the literature. We think that this is due not to the rare occurrence in Negroes but rather to either the failure of physicians to make a proper diagnosis, because of the atypical clinical appearance and the infrequency with which biopsies have been made in Negroes, or their failure to report cases observed in Negroes.

SUMMARY AND CONCLUSIONS

Three cases of lichen planus in Negroes are presented and the literature is reviewed. Pitfalls of diagnosis of lichen planus in Negroes are commented on.

Depigmentation of lesions early in the disease is due to the colliquative degeneration and resultant washing out of pigment from the epidermis. Hyperpigmentation is due to the reformation of epidermal pigment in the atrophic epidermis, the granular layer of which is practically absent.

416 North Bedford Drive.

LONG HAIR, CHIEF OF THE CROWS

EDWARD F. CORSON, M.D.
PHILADELPHIA

AMONG the races which developed and cultivated long hair in fairly recent times, those of the Mongoloid type, especially the American Indians, were notable, and among these Indians the Crow tribe had the reputation of possessing the most extensive growth. The men outstripped the women in this respect, and pride in their own hirsuties and admiration of this feature in others were to be readily noted in their ingenuous manners.

As background I quote Catlin,[1] who visited the Crows early in the last century and described them as being of fine physique and especially noted for their magnificent growth of hair. He said:

> I observed . . . that most of them were over 6 feet [183 cm.] high, and very many of these have cultivated their natural hair to such an almost incredible length, that it sweeps the ground as they walk; there are frequent instances of this kind amongst them, and in some cases, a foot or more of it will drag on the grass as they walk, giving exceeding grace and beauty to their movements. They usually oil their hair with a profusion of bear's grease every morning, which is no doubt one cause of the unusual length to which their hair extends; though it cannot be the sole cause of it, for the other tribes throughout this country use the bear's grease in equal profusion without producing the same results.
>
> The present chief of the Crows, who is called Long Hair and has received his name as well as his office from the circumstances of having the longest hair of any man in the nation, I have not yet seen: . . . This extraordinary man is known to several gentlemen with whom I am acquainted, and particularly to Messrs. Sublette and Campbell . . . who told me they had lived in his hospitable lodge for months together; and assured me that they had measured his hair by a correct means, and found it to be 10 feet and 7 inches [323 cm.] in length; closely inspecting every part of it at the same time, and satisfying themselves that it was the natural growth.

This is nonscientific evidence from members of a class of persons (travelers and traders) who were sometimes inclined to exaggerate. Nevertheless, they were practical, and their inspection and measurement are not far out of line with the statements of some others of that period, the 1830's. It constitutes the first mention, as far as I can

1. Catlin, G.: Letters and Notes on the Manners, Customs and Condition of North American Indians, ed. 3, London, Tilt & Bogue, 1842.

ascertain, of this person's unusual growth of hair. Not long afterward several other travelers noted the marvelous length of Chief Long Hair's growth, which was estimated at from 9 feet 11 inches (302 cm.) to 10 feet 7 inches (323 cm.).[2]

My interest in the subject began at a dinner of the Order of Indian Wars of the United States on Feb. 17, 1934, at which the late General Hugh L. Scott, former Chief of Staff, United States Army, and an authority on certain Indian matters, spoke and included in his talk the story of his experiences among the Crow Indians.

General Scott's remarks, according to my notes taken then, were, in part, as follows:

There was formerly a Crow chief called Long Hair on account of his remarkable growth. He wore his hair in a bag suspended from his neck. When he wished to have it brushed he went into his lodge, took it down and spread it out evenly from his head. Other Indians were brought in, sat around the edges of the lodge and combed the hair with porcupine tails. They oiled it, stroked it, then folded it toward the head and finally replaced it in the bag.

The chief died before General Scott visited the Crows, but Scott heard about him from them. He was curious about the matter but never could see any of the hair, although there were vague reports of its still existing as strands in possession of some of the Indians. It was much venerated, as the unusual growth was thought to be a sign of divinity or, at least, to possess supernatural power. The Indians were closemouthed about it. Finally General Scott heard that an Indian named Rabbit Foot had had some of it in his possession, but he, also, was dead. The hair had been buried with him. He then learned that a brave named Plenty Coups was in possession of a strand but was very secretive and easily alarmed about it if the matter was mentioned. They talked together frequently, but the general never once mentioned "hair." Had he done so that blunder would have ended the quest.

General Scott gave up all hope of ever seeing the lock. Twenty years passed. Then, in 1930, together with Mr. Scott Leavitt, chairman of the House of Representatives Committee on Indian Affairs, he was again at the Crow agency. He called on Plenty Coups and had a friendly visit. Again, there was no "hair talk." The next day he was engaged in a ceremonial visit with some other Indians when Plenty Coups came to him and invited him to come to his house the next day, saying that he would show him the hair and anything else he wished to see. He apologized for the visit of the day before and said that his lodge had not been arranged then but that now all was ready. He also invited Mr. Leavitt and a few Indian interpreters.

Mr. Leavitt[3] recently wrote me his version of the visit, which closely corresponded to General Scott's story. Combined into one narrative the account runs about as follows:

On Sept. 22, 1930, the general and the congressman visited Plenty Coups at Crow Agency, Montana. The old chief had an upper chamber in his lodge

2. Lowie, R. H.: The Material Culture of the Crow Indians, Anthrop. Papers Museum Nat. Hist. **21** (pt. 3):228, 1922.

3. Leavitt, S.: Personal communication to the author, Nov. 1, 1944.

where he kept his "medicine bundle" and other objects sacred to him. Besides the persons already mentioned, the interpreter, Max Bigman, an Indian woman and a blind Indian were present. Plenty Coups uttered a ceremonial prayer, bathed his hands, breast and arms in the smoke of a pine needle fire and rubbed his hands with beaver musk. The musk was passed around the circle of visitors preliminary to the production of the hair, which was wrapped in the form of an open circle in cloths of many colors and, finally, in buckskin. Each layer was peeled off until the lock was exposed.

Plenty Coups unwound it slowly and with the utmost reverence, letting it pass from hand to hand around the silent circle, and, as it was unrolled, Max Bigman measured it, hand over hand, for 76 hands [4] 1 finger (about 792 cm.). The general asked Plenty Coups whether the hair was spliced, and the latter was much incensed by the question. Mr. Leavitt had no doubt that it was all one strand. Had it not been the hair would not have been sacred to Plenty Coups, and it seemed to be so beyond all question. There was some reddish ceremonial paint in the hair, which was itself black or dark brown. Through the interpreter it was learned that Leavitt and Scott were the only white men to whom it had ever been shown. The Indians considered the length to have been 99 hands (about 1,006 cm.) and that most of it had been given to Plenty Coups but some to others.

Comparison of this length with that reported by the travelers and traders presented a gap. Even the lesser dimension was freakish, while the greater one was almost incredible. If the average rate of growth of scalp hair is put at 6 inches (15.24 cm.) a year it would require fifty years to arrive at such length. There would probably be less growth in infancy and old age, illness might check it and privation (a not infrequent experience among Indians of that era) could interfere with the normal production.

Long ago Pincus [5] observed that the life of a single hair (except during childhood) was from two to six years and that when cut short it grew quickly for a time (2 to 5 mm. every ten days). According to him, when hair was of middle age, stood uncut for two years and was 10 to 14 inches (25 to 36 cm.) long, the rate of growth dropped to half that figure. He estimated the average length of hair when uncut as from 22 to 28 inches (55 to 70 cm.), with 36 inches (90 cm.) an exception. To attain such length, as frequently occurred among these Indians and especially in the chief in question, there could have been no loss and renewal to any extent and no slowing down in the rate of growth.

Persons who had the opportunity to measure the hair during life might have observed a greater dimension than was present in the strands cut after death, depending on the distance from the scalp that the hair was clipped. To preserve as much length as possible, the

4. One hand is equal to 4 inches (10 cm.).

5. Pincus, J.: Hair: Its Treatment in Health, Weakness and Disease, London, Chatto & Windus, 1882.

most interesting feature, it is presumed that the hair was cut close to the scalp. The fact that the hair was described as black or dark brown would seem to indicate, though not necessarily so, that the Indian was not extremely old at the time of his death. If so, the length was attained fairly early in life. Ten feet (305 cm.), at the rate mentioned, could have been reached between the twentieth and thirtieth years without undue acceleration, provided that there was no interruption of the natural life of the hair, as Pincus suggests. Twenty-five feet (762 cm.) seems excessive. Could the "red ceremonial paint" have been there for a purpose other than decorative and have served as an adhesive in or a camouflage of splicing? Might not Plenty Coups have been sincere in his veneration, but victimized by an earlier possessor? Was Max Bigman's count somehow increased to make an intentionally impressive figure? In the darkness of the ceremonial chamber some trickery might have been imposed on the "pale faces" as, for instance, overlapping of the hairs in echelon. Speaking of the Assiniboins' hair, Catlin [6] said:

> I find the great length is produced by splicing or adding on several lengths, which are fastened very ingeniously by means of glue and the joints obscured by a sort of paste of red earth and glue, with which the hair is at intervals of every 2 or 3 inches [5 or 7.5 cm.] filled and divided into locks and slabs of an inch [2.5 cm.] or so in breadth.[7]

A last word came from Mr. Robert Yellowtail,[8] Superintendent of Crow Agency, Montana, speaking of Long Hair himself, " . . . his hair . . . was kept by Chief Plenty Coups. What happened to it when he died is not known." Apparently the last chance to investigate this particular strand has been lost forever.

COMMENT

While doubtless in books of travel and biography there exist accounts of races or persons with exaggerated growth of scalp hair, I have not encountered other possibly record-breaking instances. Hairy freaks reported in medical literature were mainly persons in whom hirsuties developed in situations in which normally only lanugo grew. Hubbard [9] wrote of a long-surviving California "forty-niner" with a beard over 7 feet (213 cm.) long, and that " . . . numerous instances are recorded where ladies' hair has attained a length of

6. Catlin,[1] p. 55.

7. Women's hair was cut as a form of punishment or when they were in mourning. The severed hair was sometimes used by splicing to increase the length of the hair of the braves in the tribes.

8. Yellowtail, R.: Personal communication to the author.

9. Hubbard, S. D.: A Treatise on Diseases of the Hair and Scalp, Philadelphia, Lea & Febiger, 1928, p. 50.

over 6 feet [183 cm.]." He gave no references to substantiate the last statement.

Savill [10] said that " . . . some writers have stated that they have seen hair 7 and 9 feet [213 and 274 cm.] long: there are frequent allusions to such cases in romantic poems and tales." I have been unable to trace any back to the original sources. Queues of the Chinese have not been mentioned as more than of floor length and were sometimes bolstered by the addition of extraneous fibers. Smith [11] said, "The . . . Chinese let theirs grow much longer than the Australian aboriginal men, whose hair is not long enough for a queue." No mention of East Indians with extraordinarily long hair was encountered. Danforth [12] and his associates did not recall instances of unusually long scalp hair. My personal recollection of the 7 Sutherland sisters, a group of women with magnificent hair reaching approximately to the floor who were exhibited to promote the sale of hair preparations, was that their tresses were somewhat over 5 feet (152 cm.) long in some instances.

We have, then, various opinions as to the actual length of the Indian's hair: General Hugh L. Scott and Scott Leavitt, 25 feet 5 inches (775 cm.), and Robert H. Lowie, summarizing the accounts of several early travelers, 9 feet 11 inches (302 cm.) to 10 feet 7 inches (323 cm.).

From the fact that this particular person stood out so prominently in this respect that even in a tribe of men excelling in growth of hair he was named Long Hair, it would seem that he had most unusual locks. Even the shortest length estimated constitutes a record in growth as far as I have been able to discover.

136 South Sixteenth Street.

10. Savill, A.: The Hair and Scalp, Baltimore, Williams & Wilkins Company, 1945, p. 20.

11. Smith, R. B.: The Aborigines of Victoria, etc., London, Trubner & Company, 1878, vol. 2, p. 243.

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ACIDITY OF THE SCALP

Nature and Possible Relation to Seborrhea

OLAF BERGEIM, Ph.D.
AND
THEODORE CORNBLEET, M.D.
CHICAGO

SEBORRHEA and seborrheic skin are poorly understood terms that defy accurate definition. Nonetheless, experienced dermatologists develop some conception of them, though they may be embarrassed about putting it in writing. The one outstanding quality, oiliness, may indeed be absent in some cases, as in the dry varieties. Scaling, too, may be present or absent. Obvious inflammation may be lacking, or a severe degree of exudation can occur. Election of sites of large and numerous oil glands is a common denominator. The laboratory observations, too, are discouraging. Diverse organisms are seen. Pityrosporum ovale, observed often on the scalp, may be present in cases of seborrhea, but this observation is not constant. We are ignorant of what else may support the seborrheal state. The diathetic, the endocrine and the vegetative nervous factors, of course, have been considered in a theoretic way. It seems obvious that the problem must be surveyed more accurately and in detail. Among the biochemical angles which were thought worthy of investigation was the question of acidity of the scalp. The greater number of the normal subjects studied were medical students, mainly young men. The influence of washing the hair with soaps and other types of shampoo was studied. The extent of seborrhea was noted. Note was made as to the use of any tonics or other applications to the scalp.

Studies of the nature of the acids involved were made on scalp washings. The hair and scalp were rinsed thoroughly with a total of 200 cc. of distilled water. Lactic acid was determined by the method of Friedemann and Graeser.[1] Total volatile acids were determined by acidification with sulfuric acid and distillation with additions of water until all volatile acids had been driven over, followed by titration with

From the Departments of Biological Chemistry and Dermatology, University of Illinois College of Medicine.

1. Friedemann, T. E., and Graeser, J. B.: The Determination of Lactic Acid, J. Biol. Chem. **100**:291-308 (March) 1933.

phenolphthalein as an indicator, after the distillates had been aerated for fifteen minutes with air free from carbon dioxide.

RESULTS

Analyses of scalp washings showed, in five tests made within twenty-four hours after washing of the scalp, average values for p_H of 5.7, for lactic acid 0.015 normal, for volatile acid 0.0011 normal, the volatile acid being 7 per cent of the total acidity. In seven tests made five to seven days after washing, the p_H was 5.2, the lactic acid 0.022 normal and the volatile acid 0.0051 normal, the volatile acid being 19 per cent of the total acidity. It is clear that the principal acid involved is lactic acid. A significant amount of volatile fatty acids was, however, also observed, amounting to from 4 to 33 per cent of the combined lactic and volatile fatty acid content. These results are similar to those obtained by us on sweat from other parts of the body and indicate that the acidity of the scalp is essentially the result of sweating at the surface of the scalp. It is interesting that a higher proportion of volatile fatty acids was noted on the scalp in tests made five to ten days after washing than in tests made when the scalp had been washed within twenty-four hours. This suggests that the volatile fatty acids are not secreted as such, but are at least largely formed on the scalp. Since our earlier studies on body sweat indicate that the volatile fatty acids are formed by bacterial action on lactic acid secreted in the sweat, it seems probable that a similar mechanism is involved here. Determinations of p_H were also carried out directly on the scalp, with glass or antimony electrodes. The 60 subjects used were mainly young men and women. Values varied from 4.3 to 6.1. The higher values were in general obtained in cases in which the hair had been washed within twenty-four hours and the lower ones in cases in which the hair had not been washed for several days. Thus, one day after washing values of 4.9 to 6.1 were obtained, with an average of 5.7. Two to four days after washing values of 4.9 to 6.0 were obtained, with an average of 5.4. After five to ten days values varied from 4.3 to 5.6, with an average of 5.1. The influence of washing was perhaps better shown by experiments made on 3 subjects at different times. These showed an average p_H the first day after washing of 5.6, after two days of 5.3, after five days of 5.2, after seven days of 4.8 and after ten days of 4.6.

The results indicate a decided effect of washing on the p_H of the scalp, showing that several days may be required for the acidity to be restored to a more or less stable value. That the reduction in acidity after washing was not due to alkalinity of the soap used was shown by the fact that washing of the scalp with shampoos not containing soap, such as K lauryl sulfates the solutions of which had an acid p_H of about 6.2, gave similar results.

That the acidity of the scalp may be responsible for a significant antibacterial action is indicated by the similarity of the acidity of the scalp to that of other surfaces of the body which have been more fully studied. We noted in previous studies [2] that the lactic acid of sweat might be expected to have a significant antibacterial action for a great variety of micro-organisms as long as the p_H was maintained at about 5.3 or below and that the volatile fatty acids might, because of their greater efficacy, extend the protection to about p_H 6.2. While the exact concentration of acid at the surface of the scalp is difficult to estimate, it nevertheless seems clear that the p_H values of 4.5 to 5.5, commonly observed on the scalp, represent acidities having a definite antibacterial action, which may well be important in the prevention of infection of the scalp. We observed, for example, that growth of Staphylococcus albus and Staphylococcus aureus was inhibited at p_H 5.4 by 0.025 normal volatile fatty acid and that Streptococcus hemolyticus was still more sensitive.[3] In fact, all the eighteen bacteria studied by us except Bacillus acidophilus were inhibited under these conditions and most of them by 0.01 normal acid at p_H 5. The protection against yeast and other fungi which are less susceptible to the influence of acid might be expected to be less than for most bacteria, but still appreciable. The flora commonly observed on the normal scalp fits in with this view, few acid-susceptible organisms being commonly observed on the scalp. It is believed, therefore, that the acidity of the scalp may serve as an important protection against infections of various types. The antibacterial action of the scalp may be somewhat reduced for the first days after washing, but may still generally be adequate since some acid sweat may be secreted almost immediately.

That some relation may exist between acidity and itching of the scalp is indicated by the fact that itching of the scalp was often associated with low p_H values and was alleviated when the scalp was washed, with associated rise in p_H. Solutions of volatile fatty acids, such as acetic acid, with p_H values of 4.5 to 5 may produce some irritation when applied to the scalp of certain persons. The acids are also the only water-soluble irritant substances known to be present in scalp washings, with the possible exception of sodium chloride. That itching is not always present with high acidities indicates that it may be observed to vary with the irritability of the scalp, which may vary with different persons and with the condition of the scalp at the moment. Also, if the cutaneous

2. Bergeim, O., and Cornbleet, T.: The Antibacterial Action of the Lactic Acid and Volatile Fatty Acids of Sweat, Am. J. M. Sc. **205**:785-792 (June) 1943.

3. Bergeim, O.: Toxicity of Intestinal Volatile Fatty Acids for Yeast and Esch. Coli, J. Infect. Dis. **66**:222-234 (May-June) 1940. Bergeim, O.; Hanszen, A. H.; Pincussen, L., and Weiss, E.: Relation of Volatile Fatty Acids and Hydrogen Sulfide to the Intestinal Flora, J. Infect. Dis. **69**:155-166 (Sept.-Oct.) 1941.

surface be damaged from any cause acidity may produce itching, which would not occur if the scalp were intact. Itching of the scalp may also occur, of course, dissociated from acidity.

The relation of the acidity of the scalp to the somewhat indefinite disease spoken of as seborrhea is not clear and will require further study. The scalps studied by us were given a careful clinical examination. No definite correlation of dandruff or other symptoms with acidity was noted, indicating that acidity is not the only factor involved. This does not exclude the possibility of acidity's being of importance at certain stages in the development of seborrhea. Because of the definite antibacterial action of such acidity it would be surprising if this were not the case. Further work will, however, be required to determine just what role acidity may play.

SUMMARY AND CONCLUSIONS

The human scalp was observed to have a distinctly acid reaction. The acidity usually varied between p_H 4.5 and 5.5. The acidity was due to lactic acid secreted in the sweat and, to a lesser degree, to volatile fatty acids which are believed to be formed from the lactic acid by micro-organisms on the scalp. The acidities observed were adequate to account for a definite antibacterial action for many types of micro-organisms and are believed to be of importance in the prevention of infections of the scalp. The accumulation of acids is believed to be not uncommonly associated with itching of the scalp, which is relieved by washing. Washing reduces the acidity temporarily. No uniform relationship was observed between acidity and seborrhea. Further work will be required to determine just what the role of acidity is in this disease.

PERSISTENT LOCALIZED BULLOUS ERUPTION ASSOCIATED WITH FOCAL INFECTION

STEPHAN EPSTEIN, M.D.
MARSHFIELD, WIS.

WITHIN one year I have encountered 2 strikingly similar instances of a persistent localized bullous eruption of the skin in elderly patients that apparently was due to focal infection of the teeth.

REPORT OF CASES

CASE 1.—Mr. W. M., a white man 70 years of age, was referred to me on Feb. 21, 1945 with a bullous eruption of his wrists of three months' duration.

History.—The patient was employed by the street department of his city. For about two years his work consisted of heating tar for roads. His wrists were always exposed to the steam from the boiling tar, and sometimes liquid tar actually splattered onto his hands and wrists. He used fuel oil to remove the tar from his skin. The patient did not have any cutaneous discomfort until the summer of 1944, when he noticed itching and an irritation of his wrists. This irritation did not clear up, even when he changed his work to shoveling snow in the winter. In December 1944 he noticed blisters on his wrists and around his ankles. This bullous eruption improved when he stopped working, but never healed completely. The patient thought that the blisters were caused by tar. He denied taking any drugs.

Examination.—Large bullae were noted around both wrists, some of them filled with pus. Healing blisters were present on both ankles. There were also crusted lesions on his back. The lesions caused only slight itching, but considerable "burning." There was no evidence of Nikolsky's phenomenon. Cultures from blisters both on plain agar and on crystal violet blood agar were negative several times. In two instances staphylococci and a few chain-forming gram-positive cocci were observed. The latter were identified as pneumococci in one instance. A smear from a blister showed 19 per cent eosinophils. The eosinophils in the blood varied from 2 to 3 per cent. Reactions to routine patch tests, including tests with coal tar, were negative. Bacterial tests elicited a severe tuberculin type of reaction to Streptococcus hemolyticus. At one time this antigen produced a central blister superimposed on the erythematous reaction, a rather unusual phenomenon. However, this phenomenon could not be duplicated. Reactions to intradermal tests with various staphylococcic antigens were negative.

The general examination revealed the teeth to be in a poor state. Roentgenograms of the teeth showed many root fragments and abscesses (fig. 2). Otherwise there were no noteworthy observations of disease.

Course of the Disease.—A tentative diagnosis of staphylococcic impetigo was made, and the usual treatment of this disease was prescribed. New blisters con-

From the Marshfield Clinic and St. Joseph's Hospital.

tinued to occur. Therefore, the patient was hospitalized on March 5, 1945. He was treated locally with silver nitrate, gentian violet medicinal and a rivanol zinc oil (2-ethoxy-6,9-diaminoacridinium hydrochloride 0.6 Gm., ichthammol 1.2 Gm., zinc oxide 24.0 Gm. and olive oil [or corn oil] to make 60.0 cc.); still new blisters appeared beneath the bandage. On account of the persistence of the lesions, the sterility of fresh blisters and the high eosinophilia of the vesicular fluid, the

Fig. 1 (case 1).—Bullous eruption of the wrist resembling staphylococcic bullous impetigo, as it appeared when the patient was first seen.

Fig. 2 (case 1).—Roentgenograms of abscessed teeth (enlarged). The abscesses can be seen as light areas around the roots (arrows).

possibility of dermatitis herpetiformis or pemphigus vulgaris was considered. Treatment with sulfapyridine did not produce any change. Treatment with sulfathiazole also was tried without success. There was slight improvement following treatment with penicillin, inasmuch as fewer new blisters appeared. At that time the possibility of a causative connection between the patient's eruption and his infected teeth was considered, and extraction of his teeth was recommended. The

patient hesitated one more month. During that time the bullous eruption continued. Then he had his remaining teeth removed. Within three to four weeks after the extraction of the teeth the blisters stopped recurring, and the patient has been well up to the time of writing (one year).

CASE 2.—A similar case was observed a year later. Mrs. M. G., 58 years of age, was referred to me on Jan. 7, 1946 because of a bullous dermatitis of the lower part of the left leg, of several months' duration.

History.—Four months before the patient had injured her left ankle. The site of this injury began to itch and swell, and a blister appeared. After this more bullae occurred, not only at the original site but also on the wrists and forearms. The patient felt well in general. She knew that she had a bad tooth, but the dentist had refused to extract it on account of her cutaneous disease. The patient did not take any drugs. Treatment by the family physician was unsuccessful. Therefore, he recommended hospitalization.

Examination.—At the time of the patient's admission to the hospital the left ankle was swollen and covered with numerous pea-sized to bean-sized blisters,

Fig. 3 (case 2).—Roentgenogram of teeth (enlarged), showing partial destruction and apical abscess of right lower bicuspid.

which extended upward along the lower part of the left leg. Redness and signs of healed blisters were noted on the wrists. There was no evidence of Nikolsky's phenomenon. The general examination revealed mild hypertension and moderately infected tonsils and teeth. The roentgenologic examination of the teeth revealed one right lower bicuspid to be partly destroyed with an apical abscess (fig. 3).

Course of the Disease.—A clinical diagnosis of bullous staphylococcic impetigo was made. Like the patient in case 1, this patient did not respond to the routine treatment for staphylococcic impetigo, although it was carried out at the hospital with utmost care. New blisters continued to occur even after the patient received penicillin, 20,000 units five times a day. However, there were fewer new bullae during the penicillin therapy. As a result of the observations in case 1, removal of the infected tooth was recommended. After the patient left the hospital more blisters appeared for a few more weeks until the infected tooth was removed. Shortly after the extraction her bullous eruption disappeared. The patient has been well up to the time of writing (three months).

COMMENT

The observations in these 2 cases seem significant for two reasons. They demonstrate again the importance of focal infection for certain dermatologic diseases and help to explain the cause of certain benign bullous eruptions.

Role of Focal Infection.—The significance of focal infection for the pathogenesis of dermatologic diseases is still a matter of discussion.[1] In my opinion focal infection plays a much greater part than is generally recognized, especially in the pathogenesis of various forms of eczema. However, it is not within the scope of this report to deal in detail with focal infection in dermatologic diseases. In the 2 cases the relationship between the bullous eruption and the infection of the teeth seems definitely established. This claim is based on the following observations. 1. Focal infection in the form of abscessed teeth had been demonstrated. 2. All local and general treatment carried on for many months proved unsuccessful. 3. Removal of the focal infection led to a rapid and permanent cure of the eruption.

A few more observations that point further to the causative role of the focal infection might be added. Among them are the bacteriologic studies carried out in case 1. The blisters apparently were not due to a direct infection of the skin. The fluid from fresh blisters was sterile. The positive smears and cultures from the content of two older blisters can be interpreted as due to secondary invaders, as it is well known that any bulla may become contaminated in time. This viewpoint is supported by the fact that in both these instances two different kinds of cocci were observed.

Most phenomena in what is called focal infection actually are due to allergy rather than infection. In the 2 cases some observations point in the direction of an allergic reaction, among them the high eosinophil count of the blister fluid and the severe partially vesicular reaction elicited by the intradermal injection of a streptococcic vaccine.

These observations and facts taken together seem to fulfil the requirements for establishing an etiologic relationship between the bullous eruption and the focal infection. Another question remains: Why did the apparently long-standing and quiet focal infection suddenly produce the bullous eruption? The answer in these 2 cases may be based on the preceding trauma. The role of trauma in regard to the localization of manifestations of focal infection is known. In both cases trauma antedated the eruption. In case 1 the bullous eruption was preceded by chronic dermatitis. The occurrence of this dermatitis during the summer months, the history of close contact with tar and

1. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 6, Philadelphia, Lea & Febiger, 1943, p. 74.

the negative reaction to the patch test with tar make it appear likely that this was dermatitis from sensitization to sunlight caused by the tar. In the second case the patient definitely reported a mechanical injury as the eliciting factor. It is noteworthy that in both instances the bullous eruption occurred originally at the exact site of the preceding trauma.

Differentiation from and Relationship to Other Bullous Eruptions.—The bullous eruptions observed in cases 1 and 2 had to be distinguished mainly from bullous staphylococcic impetigo, dermatitis herpetiformis and pemphigus vulgaris. A bullous eruption due to drugs was excluded by the history and the observation during the hospitalization of the patients.

Relationship to Bullous Staphylococcic Impetigo: Clinically these cases resembled bullous staphylococcic impetigo, although the location of the eruption was atypical. Furthermore, staphylococcic impetigo usually occurs during the hot summer months.[2] Both cases originated in late fall.

The prolonged course, the sterility of fresh blisters, the continued appearance of bullae in spite of appropriate local therapy and especially the failure of sulfonamide drugs and penicillin ruled out bullous staphylococcic impetigo.

On the other hand, the ineffectiveness of the internal treatment with sulfonamide drugs and penicillin is quite compatible with the assumption of a focal infection. Much penetration of sulfonamide drugs or penicillin from the blood stream into the root abscesses cannot be expected.

Still there seems to exist a certain relationship between the eruptions described and bullous staphylococcic impetigo. It has been demonstrated that allergic phenomena play a role in the production of bullous lesions in staphylococcic impetigo.[3] In experimental infection with material from bullous staphylococcic impetigo, bullous lesions appeared on the seventh day at the site of the inoculations. In these experiments, the incubation period and the further course demonstrated a state of localized sensitivity to staphylococci. However, in staphylococcic impetigo there is a sensitivity to a local infection, whereas in the cases herein reported the sensitivity was due to a distant focus of infection.

Relationship to Localized Bullous Dermatitis Herpetiformis: Clinically, the eruption that has been described did not resemble the typical

2. Epstein, S.: Staphylococcic Impetigo Contagiosa, Arch. Dermat. & Syph. **42**:840-855 (Nov.) 1940.

3. Epstein, S.: Local Allergic Phenomena in Circinary Impetigo: Contribution to the Etiology of Staphylococcic Impetigo Contagiosa, J. Invest. Dermat. **3**: 223-230 (June) 1940.

picture of dermatitis herpetiformis. Yet there are some factors which link these cases with dermatitis herpetiformis. There are cases of dermatitis herpetiformis that have been considered connected with focal infection.[4] Some authors[5] have expressed the belief that bacterial allergy plays a role in dermatitis herpetiformis. These investigators reported bullous reactions from intradermal injections of vaccines in their cases. In most instances these reactions occurred with Escherichia coli, but they have been also reported with Staphylococcus aureus and Streptococcus hemolyticus. I have seen in 2 instances of dermatitis herpetiformis bullous reactions from Staph. aureus. This reaction could be elicited repeatedly, though not always. Bacterial tests in hundreds of patients with dermatologic and other allergies as well as in controls have shown that bullous reactions are extremely rare with these antigens.

The case of Callaway and Sternberg[5a] is especially interesting because the patient exhibited numerous foci of infection in the lungs, teeth, tonsils and intestinal tract. In their case the removal of the teeth and tonsils produced severe flare-ups of the eruption. Desensitization with pneumococci cultured from the patient's bronchiectasis led to disappearance of the eruption, and overdoses of the vaccine apparently caused exacerbations. This case of Callaway and Sternberg is not comparable to the 2 cases of this report. But one may recognize a relationship between the atypical bullous eruption caused by a single focus of infection and the more complicated sensitization phenomena in Callaway and Sternberg's case that presented the typical picture of dermatitis herpetiformis.

I may mention, furthermore, reports of dermatitis-herpetiformis-like eruptions which apparently were bullous dermatophytids.[6]

The common denominator of these observations and the 2 cases of this report may be that of a bullous allergic reaction based on bacterial allergy.

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4. Riecke, E.: Dermatitis Herpetiformis, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 7, pt. 2, p. 549 ff.

5. (*a*) Callaway, J., and Sternberg, T. H.: Bacterial Allergy: An Etiologic Factor in Dermatitis Herpetiformis, Arch. Dermat. & Syph. **43**:956-961 (June) 1941. (*b*) Swartz, J. H., and Lever, W. F.: Dermatitis Herpetiformis: Immunologic and Therapeutic Considerations, ibid. **47**:680-693, (May) 1943.

6. Tolmach, J. A., and Schweig, J.: Generalized Trichophyton Purpureum Infection Simulating Dermatitis Herpetiformis: Report of a Case Arch. Dermat. & Syph. **41**:732-735 (April) 1940. Peck, S. M., and Rosenfeld, H.: Recurrent Bullous Eruption (Duhring's Disease?) Treated with Trichophytin, ibid. **41**:812-813 (April) 1940.

There seems, however, a much closer link between my cases and some others in which observations were described as bullous dermatitis herpetiformis. In a report on 15 cases, Goodman [7] described a type that occurs mostly in elderly persons. It consists only of bullae, usually is localized and Nikolsky's phenomenon is not present. Apparently no search for a focal infection was made in Goodman's cases. There is a similarity between some of the observations in his cases and mine. It would seem to be appropriate to look for a focal infection in future observations of this type.

Relationship to Pemphigus Vulgaris: The cases of this report did not present the typical picture of pemphigus vulgaris. But the diagnosis of a localized pemphigus always has to be considered when a bullous eruption persists and no apparent cause, such as the use of a drug, can be established. There are reports in the literature about localized benign pemphigus, usually without Nikolsky's phenomenon. I can remember several instances of disease which were so diagnosed by others or by myself and which either cleared up or at least never turned into definite pemphigus. Goodman [7] stated the belief that they were of localized bullous dermatitis herpetiformis. Here, too, investigation in regard to focal infection seems indicated.

SUMMARY AND CONCLUSIONS

Two strikingly similar cases of a persistent localized bullous eruption of the skin in older persons are reported. They resisted anti-infectious external and internal treatment for many months, but cleared up rapidly and permanently after the removal of infected teeth. This eruption is considered to be due to focal infection. It is suggested that such a pathogenesis may be the basis for some of the cases described as localized bullous dermatitis herpetiformis or benign localized pemphigus.

7. Goodman, M. H.: Bullous Dermatitis Herpetiformis, Arch. Dermat. & Syph. **46**:218-224 (Aug.) 1942.

TREATMENT OF PLANTAR WARTS

HARVEY BLANK, M.D.*
PHILADELPHIA

A HIGHLY successful method of treatment of plantar warts, without complications and without roentgen rays, is presented. Numerous methods of treatment have been proposed, but none has been entirely satisfactory. The method described in this report is simple, requires little equipment, does not disable the patient, cures a high percentage and causes no complications or painful sequelae. It is particularly useful when adequate roentgen ray therapy is not available or has failed to destroy the lesion.

The method used aims to overcome the two main problems of the treatment of plantar verrucae, namely, the inaccessibility of the lesion and the adequate destruction of its substance without producing a painful scar. The verruca is made accessible by applying a thick ring pad around the lesion so that when the patient bears weight on the foot the verruca is extruded through the hole. Adequate destruction of the lesion is accomplished with the proper application of phenol and nitric acid. Either of these drugs used alone may cause destructive changes which are unpredictable and result in injury to the patient. If they are used in combination by first applying phenol and following it immediately with nitric acid, the penetrating necrosing action is controlled by the reaction which converts the two chemicals into trinitrophenol (picric acid). The instantaneous reaction which occurs produces a tiny tough eschar in the tissue which protects the skin from further caustic action and thus gives complete control of the degree of destruction.

It should be emphasized that the chemical cauterization of plantar warts is associated with danger. These substances must be applied carefully in small amounts in order that only the lesion itself be touched and that the surrounding normal skin be undamaged. If used correctly, in accordance with the procedure described, this chemical method is safe.

METHOD AND MATERIALS

The materials necessary are a scalpel, adhesive plaster, 90 per cent phenol, concentrated nitric acid, 60 per cent salicylic acid ointment and, if possible, a piece of stiff felt.

* Formerly Major, Medical Corps, Army of the United States.
From the Department of Dermatology and Syphilology, University of Pennsylvania Medical School, Dr. Donald M. Pillsbury, Director.

STEP 1.—With a sharp scalpel or a razor blade the suspected lesion is pared down as much as possible. The diagnosis can then be confirmed by observing in the center of the callus the circumscribed verruca with several small dots in its center. These are the vascular papillae which are hypertrophied in a wart. A careful examination should also be made for satellite verrucae, which will be seen surrounding the central lesion and which are a frequent cause for failure of any method of therapy.

If vesicles or other signs of dermatophytosis are noted the treatment of the verruca must be delayed until the fungous infection is cured by other means. This is done to prevent an exacerbation of the dermatitis under the occlusive adhesive plaster.

STEP 2.—With a fine wooden applicator, a drop of 90 per cent phenol (so-called "liquefied crystals of phenol") is carefully applied to the top of the wart.

STEP 3.—With another wooden applicator, a drop of "fuming" concentrated nitric acid is applied directly over the phenol. A slight sputter is heard as the lesion turns dark brown. Practically no discomfort is experienced by the patient, although the sound may startle him at the first treatment.

STEP 4.—A rounded pad is devised with a piece of stiff felt or six to eight layers of adhesive tape. It should have tapering edges for comfort and a hole in the center which is the size of the verruca and which just fits over it. This is then applied to the foot. If multiple warts are present they can be treated by using separate pads or by having two holes in one pad.

STEP 5.—A small amount of ointment consisting of 60 per cent salicylic acid in petrolatum is placed in the ring. The ointment is used to soften the epidermis in order that it may be trimmed with ease at the time of the next treatment. The hole should not be completely filled with the ointment or it will prevent the adequate extrusion of the verruca. The entire pad, including the hole, is then covered and fastened to the foot with several strips of adhesive tape. These should be applied in such a manner that the pad cannot slip and the keratolytic ointment cannot escape.

After this treatment the patient is instructed to continue his usual activities. It is essential that the patient force the lesion into the well-like opening by walking on the pad. The use of the pad is an important part of the treatment, and it must be applied with care. To prevent it from slipping vigorous athletics, such as tennis, are prohibited. Bathing or showers are permitted, but the patient should be cautioned not to disturb the dressing.

In four or five days the dressing is removed, and the verruca with the surrounding callus is again pared down as thin as possible. At this time the skin will be observed to be white and soft from the action of the ointment. One should attempt to remove as much as possible of the dead epidermis without causing bleeding from the vascular papillae in the center of the wart. If bleeding occurs no harm is done, but several minutes should elapse to allow it to stop before the treatment is continued.

The same procedure, as previously outlined, beginning with the application of the phenol, is repeated and the lesion dressed in the same manner. Occasionally the verruca will become sensitive for the first

day or two after treatment. If this persists the treatment should be decreased by omitting the caustics or both the caustics and the ointment at the next treatment. The complete procedure can be resumed for the following treatment.

CRITERIA OF CURE

The number of times the lesion will have to be treated to obtain a cure depends largely on the age and depth of the verruca. At the completion of the treatment there must be a smooth continuity of the skin, with absence of the ring demarcating the wart from the surrounding skin, absence of the papillae in the center of the lesion and disappearance on palpation of the firm tender nodule of which the verruca is composed. The patient should be carefully examined at monthly intervals after the treatment has been completed to make certain that the lesion has not recurred.

RESULTS

The treatment described has been used on 100 patients treated under military conditions. In no instance has any serious reaction been observed. The number of applications used varied from two to twelve, the average being six. Of the 100 patients, 12 were assigned elsewhere before the period of treatment and observation could be completed. Of the 88 for whom treatment was completed and who were followed for at least one month thereafter, all but 1 were free of clinical evidence of a verruca when the course of therapy was completed.

The 1 patient for whom treatment was a failure had had repeated inadequate surgical excision and electrodesiccation over a four year period, with resultant scarring and distortion of the tissues. Of the 87 patients in whom the verrucae were obliterated by one course of treatment, 8 had a recurrence. Of these 8 patients it was possible to retreat only 5, because of military movements. But in all 5 a permanent cure was eventually obtained. It is felt that had it been possible to retreat the other 3 in whom there were recurrences, even a higher percentage of cures would have been effected.

SUMMARY

A specific and effective technic for the ambulatory treatment of plantar verrucae is described. It consists essentially of exposing the verruca with a ring pad and salicylic acid ointment and destroying it with phenol and nitric acid used successively. Although indiscriminate chemical cauterization of these lesions is not without danger, 100 consecutive patients were treated with the technic outlined with no untoward results. Eighty-four of the 88 patients (95 per cent), on whom follow-up examinations were possible, obtained a cure with this method.

A search of the available dermatologic and orthopedic literature did not reveal reference to this procedure.

CHEMISTRY OF PALMAR SWEAT

II. Chloride

WALTER C. LOBITZ Jr., M.D.
HANOVER, N. H.
AND
ARNOLD E. OSTERBERG, Ph.D.
NORTH CHICAGO, ILL.

THE CHLORIDE content of general body or thermal-regulating sweat has been studied by many observers [1] under various conditions of increased temperature, humidity and work in both hot climates and thermal chambers. Values for chloride in the sweat, as previously reported, range from 52 to 700 mg. of sodium chloride in 100 cc. of sweat. The average, however, is about 250 mg. in 100 cc.

The studies on thermal-regulating sweat are important, because they contribute much to the knowledge of loss of chemicals and water from the body as a whole. However, they give only limited information on what the sweat gland itself can do. In other words, the study of profuse dilute general body sweat contributes to the knowledge of the skin in the same way that the study of renal function during profuse diuresis contributes to the knowledge of the kidney.

From the Section on Dermatology and Syphilology (Dr. Lobitz) and the Department of Medicine, Abbott Laboratories, North Chicago, Ill. (Dr. Osterberg).

1. Fishberg, E. H., and Bierman, W.: Acid-Base Balance Sweat, J. Biol. Chem. **97**:433-441 (Aug.) 1932. Talbert, G. A., and Haugen, C. O.: Simultaneous Study of the Constituents of the Sweat, Urine and Blood, Also Gastric Acidity and Other Manifestations Resulting from Sweating: I. Chlorides, Am. J. Physiol. **81**: 74-80 (June) 1927. Adolph, E. F.: The Nature of the Activities of the Human Sweat Glands, ibid. **66**:445-452 (Nov.) 1923. Hancock, W.; Whitehouse, A. G. R., and Haldane, J. S.: The Loss of Water and Salts Through the Skin, and the Corresponding Physiological Adjustments, Proc. Roy. Soc., London, s.B **105**:43-59 (June 4) 1929. Moss, K. N.: Some Effects of High Temperatures and Muscular Exertion upon Colliers, ibid. **95**:181-200 (Aug.) 1923-1924. Whitehouse, A. G. R.: Further Investigation of Sweating and Sweat, ibid. **108**:326-339 (June 1) 1931. Berry, E. Ueber die Abhängigkeit des Stickstoff- und Chlorgehaltes des Schweisses von der Diät, Biochem, Ztschr. **72**:285-302, 1916. Hunt, E. H.: The Regulation of Body Temperature in Extremes of Dry Heat, J. Hyg. **12**:479-488, 1912. Dill, D. B.; Jones, B. F.; Edwards, H. T., and Oberg, S. A.: Salt Economy in Extreme Dry Heat, J. Biol. Chem. **100**:755-767 (May) 1933. Daly, C., and Dill, D. B.: Salt Economy in Humid Heat, Am. J. Physiol. **118**:285-289 (Feb.) 1937. Dill,

(Footnote continued on next page)

Since it is important to dermatologists and to physiologists to know just what type of work a normal sweat gland is capable of doing, this investigation of the collection and analysis of sweat was undertaken.

As previously reported,[2] the palmar sweat glands were selected for study since the nature of their physiologic functions and the position of their duct openings made it possible to collect sweat which was free from contamination by surface cells, oils and bacteria. With the chamber specially designed for these studies,[2] it is possible to see the opening of the individual sweat duct during the period of collection, and thus the manner and rate of secretion of sweat can be observed.

For the studies on chloride in sweat reported in this paper the same procedures were followed as described in the preliminary report[2]: sweat was collected from fifty glands for thirty minutes, urine was collected for the same period and a sample of venous blood was drawn at the conclusion of the period. The work was carried out during cool or cold months of the year. An interval of at least two days elapsed between repeated studies on the same person. The volumes of sweat were measured by the manipulative technic of

D. B.; Hall, F. G., and Edwards, H. T.: Changes in Composition of Sweat During Acclimatization to Heat, ibid. **123**:412-419 (Aug.) 1938. Usher, B.: Human Sweat as a Culture Medium for Bacteria, Arch. Dermat. & Syph. **18**:276-280 (Aug.) 1928. Peck, S. M.; Rosenfeld, H.; Leifer, W., and Bierman, W.: Role of Sweat as a Fungicide, with Special Reference to the Use of Constituents of Sweat in the Therapy of Fungous Infections, ibid. **39**:126-146 (Jan.) 1939. Favre, A., cited by Way and Memmesheimer. Mosher, H. H.: Simultaneous Study of Constituents of Urine and Perspiration, J. Biol. Chem. **99**:781-790 (Feb.) 1933. Mickelsen, O., and Keys, A.: The Composition of Sweat, with Special Reference to the Vitamins, ibid. **149**:479-490 (Aug.) 1943. Keutman, E. H.; Bassett, S. H., and Warren, S. L.: Eectrolyte Balances During Artificial Fever with Special Reference to Loss Through Skin, J. Clin. Investigation **18**:239-250 (March) 1939. Way, S. C., and Memmesheimer, A.: The Sudoriparous Glands: III. Sweat, Arch. Dermat. & Syph. **41**:1086-1107 (June) 1940. McCance, R. A.: The Effect of Salt Deficiency in Man on the Volume of the Extracellular Fluids, and on the Composition of Sweat, Saliva, Gastric Juice and Cerebrospinal Fluid, J. Physiol. **92**:208-218 (March) 1938. Mezincescu, M.: A Phase of Problem of Acclimatization to High Temperatures, J. Indust. Hyg. & Toxicol. **19**:146-151 (March) 1937. Hardt, L. L., and Palmer, A.: Studies in Intermittent Heat Sweats: The Chlorides and Acid-Base Balance, Am. J. Digest. Dis. **4**:489-492 (Oct.) 1937. Kuno, Y.: The Physiology of Human Perspiration, London, J. & A. Churchill, Ltd., 1934, chap. 8, pp. 176-177. McSwiney, B. A.: The Composition of Human Perspiration, Proc. Roy. Soc. Med. **27**:839-848 (May) 1934. Cohen, E. L.: Generalised Hyperidrosis, St. Barth. Hosp. J. **48**:83-84 (June) 1944.

2. Lobitz, W. C., Jr., and Osterberg, A. E.: Chemistry of Palmar Sweat: Preliminary Report; Apparatus and Technics, J. Invest. Dermat. **6**:63-74 (Feb.) 1945.

Richards, Bordley and Walker,[3] and analyses for sodium chloride in the sweat were made by the capillary tube colorimetry method described by Westfall, Findley and Richards.[4] The estimations of sodium chloride in the urine and blood plasma were made by the method of Osterberg and Schmidt.[5]

Twenty normal subjects between the ages of 19 and 38 years were studied. Eleven subjects were women and 9 were men. Forty-seven successful collections and analyses were carried out (table).

As the personalities of different persons and the moods of each person vary, so does the output of palmar sweat vary in the same and in different persons. By observing the openings of the sweat ducts during the thirty minute collection of sweat we noted that the size of sweat droplets varied from gland to gland and stimulus to stimulus in the same and in different persons. Therefore the correlation of volume output and dissolved substances would yield varying information, and 2 persons could not be compared as to volume of sweat secreted. However, the manner in which the sweat was secreted could be consistently classified as one of three main physiologic types, and individual collections could be compared on this basis.

The three main physiologic types are as follows: Type I represents profuse sweating during the entire thirty minute period. The sweat gland never rested. This is the type of sweating encountered in thermal-regulating sweat, and it might be compared to diuresis in the kidney. Type III represents repeated secretion of moderate to small amounts of sweat, with periods when the sweat gland is at rest; in other words, the sweat came intermittently. Type II combines the features of type I and type III. There was profuse sweating during the first five to ten minutes and little intermittent sweating during the remaining period. In figure 1 the collections are represented graphically according to physiologic type.

In the earlier study twenty successful collections from 6 normal subjects (4 men and 2 women) were made. Of these collections four were type I, one was type II and fifteen were type III. By adding these twenty collections to the collections made in this study we have a total of sixty-seven successful collections of sweat for analysis of chloride (resulting from one hundred and seven attempts). Thirty-

3. Richards, A. N.; Bordley, J., III, and Walker, A. M.: Quantitative Studies of the Composition of Glomerular Urine: VII. Manipulative Technique of Capillary Tube Colorimetry, J. Biol. Chem. **101**:179-191 (June) 1933.

4. Westfall, B. B.; Findley, T., and Richards, A. N.: Quantitative Studies of the Composition of Glomerular Urine: XII. The Concentration of Chloride in Glomerular Urine of Frogs and Necturi, J. Biol. Chem. **107**:661-672 (Dec.) 1934.

5. Osterberg, A. E., and Schmidt, E. V.: The Estimation of Plasma Chlorides, J. Lab. & Clin. Med. **13**:172-175 (Oct.) 1927.

Subject	Age, (Years), Sex	Physiologic Type of Sweating	Volume of Sweat Collected from 50 Glands in 30 Min. in 0.35 Mm.* Tube, Mm.	Volume of Urine, Cc. per Min.	Chloride		
					Sweat	Urine	Plasma
					Mg. per 100 Cc.	Sodium Chloride	
J. M.	21	III	1.00	3.60	1,000	322	600
	♀	III	0.35	0.38	780	1,263	607
		I	1.00	4.30	460	281	594
H. F.	28	III	1.00	0.52	1,200	854	598
	♂	III	0.80	1.20	1,080	632	590
		III	1.30	1.30	1,020	1,310	587
E. G.	28	III	0.80	0.48	880	854	621
	♀	II	3.70	0.40	680	1,521	590
		III	1.00	0.64	760	1,451	589
R. T.	28	II	2.00	0.44	440	1,217	615
	♂	III	1.10	0.59	760	1,474	611
B. R.	28	II	4.00	0.53	460	842	600
	♀	II	1.00	1.40	460	538	623
		II	1.50	1.80	460	304	598
M. B.	19	III	0.60	0.025	780	1,100	615
	♀	II	0.80	0.44	300	1,544	615
		II	0.70	0.10	780	1,264	587
U. S.	31	III	1.00	1.30	1,460	819	594
	♂	III	0.60	0.44	600	1,147	587
P. R.	27	III	1.20	0.40	960	1,708	594
	♂	I	1.60	0.49	615	1,685	617
		III	0.50	0.30	1,200	1,451	598
J. L.	27	III	0.40	1.20	1,520	1,310	598
	♂						
M. D.	22	II	0.70	0.40	600	1,240	573
	♀	III	0.50	0.67	1,080	1,357	607
		III	0.30	1.41	1,000	257	581
E. L.	28	I	2.20	0.37	320	1,381	598
	♀	III	1.00	0.24	760	913	598
M. M.	20	II	0.80	1.70	330	866	598
	♂	II	0.55	0.82	630	1,661	623
		III	0.40	0.57	1,040	1,310	604
J. S.	28	III	0.45	0.32	1,640	1,006	637
	♀						
H. H.	28	III	0.50	0.47	1,500	1,217	611
	♀						
G. P.	32	II	1.80	0.66	225	1,240	627
	♀	II	0.65	0.60	400	1,123	598
		II	0.30	0.50	650	1,123	611
R. T.	38	III	0.40	0.64	1,040	1,708	600
	♀	III	0.40	0.80	1,480	679	598
A. P.	22	II	6.00	1.40	215	819	594
	♀	II	0.70	1.00	300	1,264	598
		III	0.30	0.39	990	1,474	617
C. G.	24	III	0.40	0.40	1,440	1,147	604
	♂						
P. M.	33	III	0.30	0.30	1,640	1,720	617
	♂	III	0.45	0.51	1,560	1,451	600
L. R.	28	III	0.40	0.60	1,220	1,638	611
	♂	III	0.80	1.02	1,095	1,310	627
		II	0.45	0.76	600	1,264	615

* Inside diameter.

six of the collections of sweat were from women, and thirty-one were from men. The distribution as to physiologic type of sweating was as follows: type I, seven; type II, seventeen, and type III, forty-three.

In figure 2 the mean values and range of chloride secreted in the sweat in the sixty-seven analyses are represented graphically according to the three normal physiologic types. The values for chloride in urine and blood plasma for the same periods are also shown.

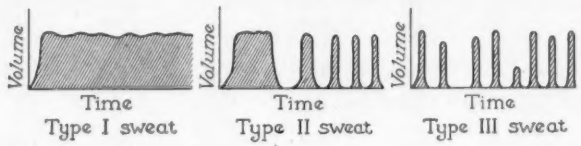

Fig. 1.—The manner of sweat output from an individual sweat gland; the so-called three physiologic types of sweating encountered.

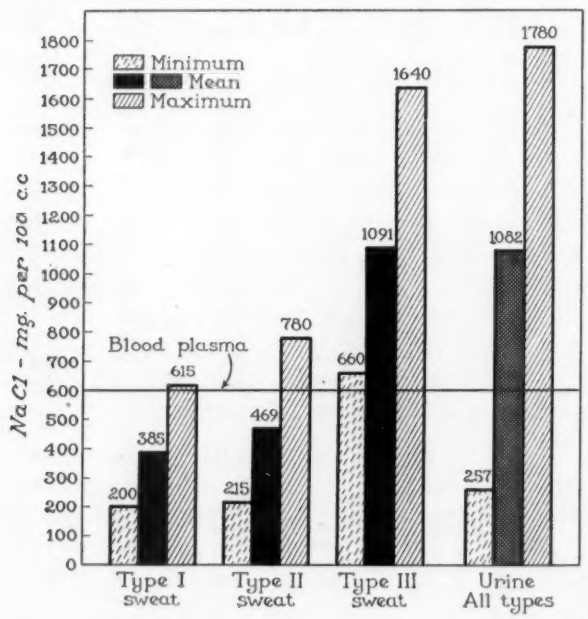

Fig. 2.—The mean values of chloride (expressed as sodium chloride) with minimum and maximum for the three physiologic types of sweating the urine in all types and the mean sodium chloride of the blood plasma in all types.

The mean value of 385 mg. of sodium chloride in 100 cc. (minimum 200 mg., maximum 615 mg.) in type I sweat agrees with the levels of sodium chloride reported in thermal-regulating or general body sweat, indicating that there are a sweat glomerulus and a tubule during the equivalent of diuresis.

A mean value for sodium chloride of 469 mg. per hundred cubic centimeters (minimum 215 mg., maximum 780 mg.) is observed in type II sweat. In this type the sweat gland may be regarded as a secreting unit partly in the equivalent of diuresis and partly not, but the greatest volume of output is during the so-called diuretic phase.

In type III the glomerulus and the tubule of the sweat gland work periodically and are shown to concentrate chloride as efficiently as the excreting units of the kidney. The mean value of sodium chloride is 1,091 mg. per hundred cubic centimeters (minimum 660 mg., maximum 1,640 mg.).

The values for chloride in the plasma were all within normal limits. The mean value of sodium chloride was 600 mg. per hundred cubic centimeters of plasma.

Readings of barometric pressures and of wet and dry bulb temperatures, in the laboratory as well as outside, during each collection showed these factors to have no correlation with the volume, physiologic type or concentration of chloride of the collected sweat.

SUMMARY AND CONCLUSIONS

By microscopic observation of duct openings of palmar sweat glands it is possible to classify the manner in which sweat is secreted into three main physiologic types: profuse, intermittent and a combination of profuse and intermittent.

The mean value of chloride (as sodium chloride) of sweat collected directly from duct openings of palmar sweat glands was 385 mg. per hundred cubic centimeters in profuse sweating, 469 mg. in the combined type of sweating and 1,091 mg. in the intermittent type of sweating. There was no correlation between these values and the content of sodium chloride in simultaneously collected blood (mean 600 mg. per hundred cubic centimeters) and urine (mean 1,082 mg. per hundred cubic centimeters).

The previously reported mean value of sodium chloride of about 250 mg. per hundred cubic centimeters of thermal-regulating, or general body, sweat agrees with the mean value of the profuse type of palmar sweat reported here.

The results of these studies give evidence that the palmar sweat gland can concentrate chloride to a greater degree than has been previously appreciated.

STUDIES ON SENSITIVITY TO FORMALDEHYDE-TREATED STARCH

HELEN RELLER GOTTSCHALK, M.D.
ST. LOUIS

THE NOXIOUS effect of talcum as used in surgeons' gloves has been stressed in the recent surgical literature.[1] This nonabsorbable powder causes a pronounced foreign body reaction in traumatized tissue and in the body cavities of both man and experimental animals (chest, abdomen, rectum, uterus, vagina). The commonest form of this reaction is chronic inflammation of the granulomatous type, progressing to the final stage of fibrosis, which when it occurs in the body cavities leads to the formation of more or less dense adhesions.

In view of these by-effects of talcum, a substitute powder has been recommended.[1a] This substitute is commercial corn starch, which as a result of treatment with formaldehyde has undergone a change in molecular structure. This change completely robs the starch of its gelatinizing properties, so that even when boiled or steamed in an autoclave it remains a free-flowing dusting powder.

The problem immediately calling for solution was the establishing of facts as to whether or not this material was comparatively innocuous, primarily irritating or capable of producing contact dermatitis after use on the skin. Patch tests were performed toward these ends.

The treated starch is prepared in the following way: Corn starch is subjected to formaldehyde vapor, under specific conditions of moisture, pressure and temperature. The free formaldehyde is then removed by washing or other suitable processes. This formaldehyde-treated starch produces no pathologic tissue response when applied to the skin or mucous membranes or injected into wounds or into the body cavities of experimental animals.[1bc] No pathologic tissue response is produced

From the Dermatological Department of the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University.

1. (*a*) Seelig, M. G.: Talcum as an Operating Room Hazard, South. M. J. **38**:470-472 (July) 1945. (*b*) Seelig, M. G.: Verda, D. J., and Kidd, F. H.: The Talcum Powder Problem in Surgery and Its Solution, J. A. M. A. **123**:950-954 (Dec. 11) 1943. (*c*) Seelig, M. G., and Verda, D. J.: The Talcum Powder Problem, J. Mt. Sinai Hosp. **12**:655-666 (May-June) 1945. (*d*) Seelig, M. G.: Abdominal Silicosis (Due to Talcum Powder) and Cancer, S. Clin. North America **24**:1162-1171 (Oct.) 1944.

when it is injected into the anterior chamber of the rabbit's eye.[2] It seems that it is almost immediately acted on by the normally present diastase of the body fluids, converted into a saccharide and absorbed.

The type of testing performed has been designated as the "prophetic patch test" technic by Dr. Louis Schwartz and Dr. Samuel Peck, of the United States Public Health Service,[3] and was recommended by them for use in foretelling whether or not a substance will produce dermatitis after contact with the skin. Two separate tests are made, ten to fourteen days apart, on the same person. Two hundred persons are used just as in other standard studies with patch tests. It is presumed that reactions will occur in the first series if the substance tested is a primary irritant, provided that the person under observation has never had previous contact with the substance. The reactions induced by the second series of tests indicate the number of persons in whom sensitivity has been induced by the first patch test.

PROCEDURE IN PATCH TESTS

Three materials were used for the patch tests: (1) the formaldehyde-treated starch before it had been autoclaved for use in the operating room, (2) talcum (Merk & Co., Inc.) and (3) plain corn starch ("argo"). The plain corn starch ("argo") and talcum served as controls for the formaldehyde-treated starch.

A group of 208 volunteers was tested. These volunteers were employees and patients at the Barnard Free Skin and Cancer Hospital and patients at the St. Louis City Hospital, the Jewish Hospital and the Barnes Hospital. No patient suffered from systemic disease; most of them were from wards for patients with fracture. No one with cutaneous disease was tested. The ages of the volunteers ranged from 14 to 70 years, the average age being 47.8 years. The sexes were fairly equally represented. There were 102 women and 106 men. Eight of the patients were Negroes.

Technic.—1. The talcum, the plain starch and the treated starch were moistened with water and applied to pieces of gauze ¼ inch (0.64 cm.) square and covered with standard "elastopatch" (Duke Manufacturing Company). 2. Patches were placed on the skin of the scapular and infrascapular areas, on the back of the arms and on the anterior and internal surfaces of the thighs (the back of the arms was the usual location). 3. Patches were removed approximately forty-eight hours later and the areas observed. The areas were again observed in ninety-six and one hundred and ten hours after the removal

2. Seelig, M. G.: Personal communication to the author.

3. Schwartz, L., and Peck, S. M.: The Patch Test in Contact Dermatitis, Pub. Health Rep. **59**:546-557 (April 28) 1944.

of the patches. 4. Ten days or more after the patches were removed, fresh ones were applied at the same sites and steps 2 and 3 were repeated.

RESULTS

There was one positive reaction in the patch tests among the 208 volunteers. This patient did not react to the material patches when the patches were applied for the first time, but after the removal of the second group of patches, a positive [4] reaction of 2 plus was observed at the area where the treated starch had been applied. One week later this patient had a patch test with 5 per cent formaldehyde and was observed to be sensitive (3 plus positive). An interesting but none the less somewhat confusing aspect of the test on this particular person is that although she was not sensitive to formaldehyde starch in the first patch test and was sensitive in the second to pure 5 per cent formaldehyde solution, she did not react positively to formaldehyde starch in a third patch test.

SUMMARY

Patch tests were performed with a formaldehyde-treated starch. Untreated starch and talcum were used as controls. The "prophetic patch test" technic was used. Two hundred and eight volunteers were tested. No positive reactions were observed after the removal of the first series of patches. One positive reaction to the formaldehyde-treated starch was observed after the removal of the second series of patches. The 1 volunteer who reacted to this starch was observed to be sensitive to formaldehyde on further testing, but did not react positively in a third patch test with formaldehyde starch.

4. One plus was a reaction of erythema, 2 plus erythema and edema, 3 plus erythema, papules and a few vesicles and 4 plus erythema, edema, many vesicles and in some cases ulceration.

EFFECTS OF ROENTGEN RAY IRRADIATION ON THE TESTES OF RABBITS

Possible Harmful Effects on Human Testes from Low Voltage Roentgen Ray Therapy

J. LAMAR CALLAWAY, M.D.

VINCE MOSELEY, M.D.

AND

SHERWOOD W. BAREFOOT, M.D.

DURHAM, N. C.

THE POSSIBILITY of damaging effects to the body of patients caused by low voltage roentgen ray therapy administered for dermatologic conditions is a constant problem to dermatologists. Radiation directed to the scrotum and adjacent areas in 4 male patients was said to have caused sterility, and in 2 other male patients it was thought likely that sterility had been produced by treatment with roentgen rays.[1] Although the amount of roentgen ray therapy given the patients was not stated, it was presumed that the treatments were responsible for their sterility. Since information is available concerning the tolerated dose of roentgen ray irradiation for human ovaries[2] but seems to be lacking in regard to human testes, it is difficult to evaluate such a report. It is well known, however, that in animals the spermatogonia and the fully developed spermatozoa in the semen, seminal vesicles or testes are more resistant to roentgen irradiation than are the spermatocytes or spermatids.[3] It has been shown, also, that fertile spermatozoa may be

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From the Division of Dermatology and Syphilology of the Department of Medicine, Duke University School of Medicine, Durham, N. C.

1. Hughner, M.: Sterility and the X-Rays, J. A. M. A. **104**:1808-1809 (May 18) 1935.

2. (*a*) Westing, S. W.: The Importance of a New X-Ray Effect for Our Daily Diagnostic and Therapeutic X-Ray Work, New York State J. Med. **40**: 1139-1144 (Aug. 1) 1940. (*b*) Mayer, M. D.; Harris, W., and Wimpfheimer, S.: Therapeutic Abortion by Means of X-Ray, Am. J. Obst. & Gynec. **32**:945-957 (Dec.) 1936. (*c*) Harris, W.: Therapeutic Abortion Produced by the Roentgen Ray, Am. J. Roentgenol. **27**:415-419 (March) 1932. (*d*) Peck, W. S.; McGreer, J. T.; Dretzchwar, N. R., and Brown, W. E.: Castration of the Female by Irradiations, Radiology **34**:176-186 (Feb.) 1940.

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observed in the semen of animals for periods as long as six to twelve weeks after administration of known sterilizing doses of roentgen rays to the testes.[4]

With many of the dangers inherent in low voltage roentgen ray therapy obviated by the use of modern types of x-ray tubes and equipment,[5] we have attempted to determine whether or not the potential danger of accidental injury to the gonadal tissues of men actually exists. The intensity of roentgen rays in scattered irradiation in air to which gonads might be exposed during the course of low roentgen ray irradiation of the face has been measured. The effect of direct roentgen ray irradiation on the testes of rabbits and the effect of direct roentgen ray irradiation on human testes have been studied.

STUDIES ON THE INTENSITY OF SCATTERED IRRADIATION

An adult-sized plastic dummy was employed as a subject for the studies on scattered irradiation. The dummy was placed on a standard x-ray table with its long axis lying at an angle of 90 degrees to the beam of roentgen rays. A technic of irradiation was used that would ordinarily be employed in the treatment for acne vulgaris of the face. A Victoreen roentgen meter was then arranged to record the intensity of the scattered irradiation in the air at a distance of 75 cm. from the point at which the x-ray tube was focused (fig. 1). This distance was used because it represents the average distance from the face to the gonadal region in most men. A standard Westinghouse "dermadex" shock-proof x-ray machine with valve-tube rectification was used in generating the irradiation. The x-ray tube used was a standard Westinghouse x-ray tube with a half-value layer of 0.35 mm. of aluminum. The formula for irradiation was 85 kilovolts, 3 milliamperes, no filter and a tube distance of 10 inches (25.4 cm.). The x-ray machine was

3. (*a*) Oslund, R. M., and Bachem, A.: Geminal Epithelium in X-Rayed Testes of Rats, Proc. Soc. Exper. Biol. & Med. **23**:761 (April) 1926. (*b*) Warren, S. L.: The Physiologic Effects on Roentgen Radiation upon Normal Body Tissues, Physiol. Rev. **8**:92-129 (Jan.) 1928. (*c*) Snyder, L. H.: Roentgen Ray Induced Sterility and the Production of Genetic Modifications, Am. J. Roentgenol. **14**: 241-243 (Sept.) 1925. (*d*) Hooker, D. R.: The Effect of Exposure to Roentgen Rays on Reproduction in Male Rats, ibid. **14**:327-336 (Oct.) 1925. (*e*) Gatenby, J. B., and Wigoder, S. B.: The Effect of X-Radiation on the Spermatogenesis of the Guinea Pig, Proc. Roy. Soc., London, s. B **104**:351-370 (March) 1929. (*f*) Asdell, S. A., and Warren, S. L.: The Effect of High Voltage Roentgen Radiation (200 kv.) upon the Fertility and Motility of the Sperm of the Rabbit, Am. J. Roentgenol. **25**:81-84 (Jan.) 1931.

4. (a) Snell, G. D.: X-Ray Sterility in the Male House Mouse, J. Exper. Zoöl. **65**:421-441 (July 5) 1933. (*b*) Strandskov, H. H.: Effects of X-Ray on Inbred Strain of Guinea Pigs, ibid. **63**:175-202 (Aug. 5) 1932.

5. Taylor, L. S.: X-Ray Protection, J. A. M. A. **116**:136-140 (Jan. 11) 1941.

calibrated by a reputable physicist immediately before the studies were undertaken. Using the formula described, an output of 100 r per minute, measured in air, might be expected.

Repeated calculations with the Victoreen roentgen meter showed that with the conditions stated each 100 r directed to the face of the dummy resulted in an intensity of 0.034 r of scattered irradiation, measured in air, 75 cm. from the center of the roentgen ray beam. Since the average patient receiving roentgen ray therapy to the face receives not more than sixteen treatments of 100 r to each side of the face, a total of thirty-two exposures might be hypothecated. Assuming that the maximum of thirty-two exposures might be used in a given person, only 1.088 r (32 x .034 r) would be expected to reach the scrotal area during the entire series of thirty-two treatments.

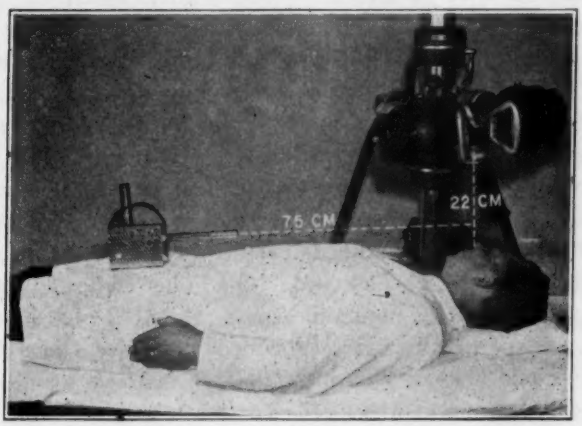

Fig. 1.—Technic used in measuring scattered irradiation.

STUDIES ON THE EFFECTS OF ROENTGEN RAYS ON RABBITS' TESTES

Our interest has been not only concerning how much roentgen ray therapy is required to sterilize animals completely but also concerning the amount required definitely to suppress spermatogenesis. We have undertaken to study the effects of varying amounts of roentgen rays in unfiltered low voltage roentgen ray therapy on the testes of rabbits. The number of spermatocytes, spermatids and spermatozoa in material aspirated from the testes was used as an index of the status of spermatogenesis. The technic employed consisted of irradiation of the testes with varying amounts of roentgen rays and, subsequently, studying microscopically material aspirated from the testes for evidence of the existing state of the spermatogenesis.

Five adult male white rabbits from the same litter were selected. Four of them were exposed to varying amounts of roentgen ray irradiation in gradually increasing doses (total dosage, 950 to 1,500 r).

When the animals were irradiated, they were placed on their backs in such a position that the roentgen ray beam would focus directly on the testes. The adjacent areas of the body were carefully screened with lead foil. The fifth rabbit was given no roentgen ray irradiation, but was examined at the same intervals as the irradiated rabbits and served as a control to eliminate the possibility of any harmful effect on spermatogenesis by the repeated aspiration of the testes. The control animal's spermatogenesis remained unchanged during the period of observation. The animals were kept in separate cages to prevent loss of spermatozoa through sexual acts.

At varying intervals an aspiration biopsy of the testes was made by inserting a 20 gage intravenous needle. A syringe containing 0.1 cc. of isotonic solution of sodium chloride was attached to the needle, and the solution was injected into the testicle, after which the plunger of the syringe was withdrawn by gentle traction. The needle was then withdrawn, and the material which had been aspirated was expelled on a warm glass slide, which was covered with a cover glass and rimmed with petrolatum, and examined under the high dry lens of a microscope. No staining methods were used. Sterile precautions were employed in the insertion of the needle into the testicle, and no infections were noted. The microscopic observations were recorded in terms of 1, 1 plus, 2 plus, 3 plus and 4 plus. Zero signified that no spermatocytes or spermatids or spermatozoa could be observed. One plus indicated only a few spermatids and motile or nonmotile spermatozoa; 2 plus indicated that spermatocytes, spermatids and spermatozoa were seen in at least every other microscopic field; 3 plus indicated spermatocytes and spermatids in every field and one to five motile spermatozoa, and 4 plus indicated that a normal number of germ cells were seen.

Observations were made at intervals over a period of eight months and were discontinued only after it was felt that a permanent arrest of spermatogenesis had occurred. Table 1 represents the observations on the entire group of animals, and the courses of the individual rabbits treated with roentgen rays are represented in graphs 1, 2, 3 and 4 in figure 2.

It can be seen that after 300 to 400 r of irradiation to the testicles deleterious suppressive effects on spermatogenesis could be recognized. However, at least 600 to 650 r are necessary before an arrest in spermatogenesis occurs. This arrest seems temporary. Nine hundred and fifty to 1,500 r are required to produce a permanent arrest in spermatogenesis.

Previous studies have shown that in mice 100 r to the testicles will induce a temporary suppression in spermatogenesis, but 800 to 1,600 r are necessary to induce sterility.[4a] Studies on guinea pigs have shown that from 422 to 864 r are required to produce temporary sterility.[4b] In rats at least 750 r are required to produce definitely recognizable depres-

TABLE 1.—*Details of Roentgen Ray Irradiation and Sperm Counts*

Day of Experiment	Rabbit 1			Rabbit 2			Rabbit 3			Rabbit 4			Control Rabbit	
	Dosage (r) Given	Total Dosage (r) to Date	Sperm Count	Dosage (r) Given	Total Dosage (r) to Date	Sperm Count	Dosage (r) Given	Total Dosage (r) to Date	Sperm Count	Dosage (r) Given	Total Dosage (r) to Date	Sperm Count	Dosage Given	Sperm Count
1	200	200	4+	50	50	4+	100	100	4+	400	400	4+	...	4+
4	...	200	2+	...	50	4+	...	100	3+	...	400	2+	...	4+
11	...	200	3+	...	50	4+	...	100	3+	...	400	2+	...	...
28	200	400	...	200	200	...	200	300	...	200	600	...	...	4+
30	...	400	4+	...	250	4+	...	300	2+	...	600	0	...	...
33	150	550	...	200	450	...	200	500	...	...	600	...	...	...
35	...	550	2+	...	450	2+	...	500	2+	...	600	0	...	3+
37	50	600	...	50	500	...	50	550	...	...	600	0	...	...
39	...	600	4+	...	500	1+	...	550	1+	...	600	...	...	2+
42	75	675	...	75	575	...	75	625	...	...	600	...	...	...
44	...	675	1+	...	575	0	...	625	1+	...	600	...	...	4+
48	75	750	...	...	575	...	50	675	...	...	600	...	...	...
50	...	750	2+	...	575	1+	...	675	1+	...	600	0	...	2+
56	75	825	...	75	650	...	75	750	...	...	600	0	...	...
58	...	825	0	...	650	0	...	750	0	...	600	...	...	Bloody tap
64	...	825	0	...	650	0	...	750	0	...	600	0	...	...
122	75	900	3+	...	650	0	...	750	1+	...	600	0	...	4+
141	...	900	3+	...	650	0	75	825	...	...	600	2+	...	...
149	...	900	2+	...	650	1+	...	825	1+	...	600	2+	...	4+
157	300	1,200	...	300	950	...	300	1,125	...	300	900	...	...	4+
168	300	1,500	2+	...	950	0	...	1,125	0	...	900	2+	...	4+
187	...	1,500	0	...	950	0	...	1,125	0	300	1,200	0	...	...
215	...	1,500	0	...	950	0	...	1,125	0	...	1,200	0	...	4+
238	...	1,500	0	...	950	0	...	1,125	0	....	1,200	0	...	4+

sion of spermatogenesis.[6] Studies on the albino rat have shown that recovery from suppressed spermatogenesis is slow with 800 r and rare with 1,000 to 1,200 r, and when spontaneous regeneration occurs spermatozoa are rarely produced. Spontaneous regenerative changes are temporary, and involution follows fifty to eighty days after irradiation.[7]

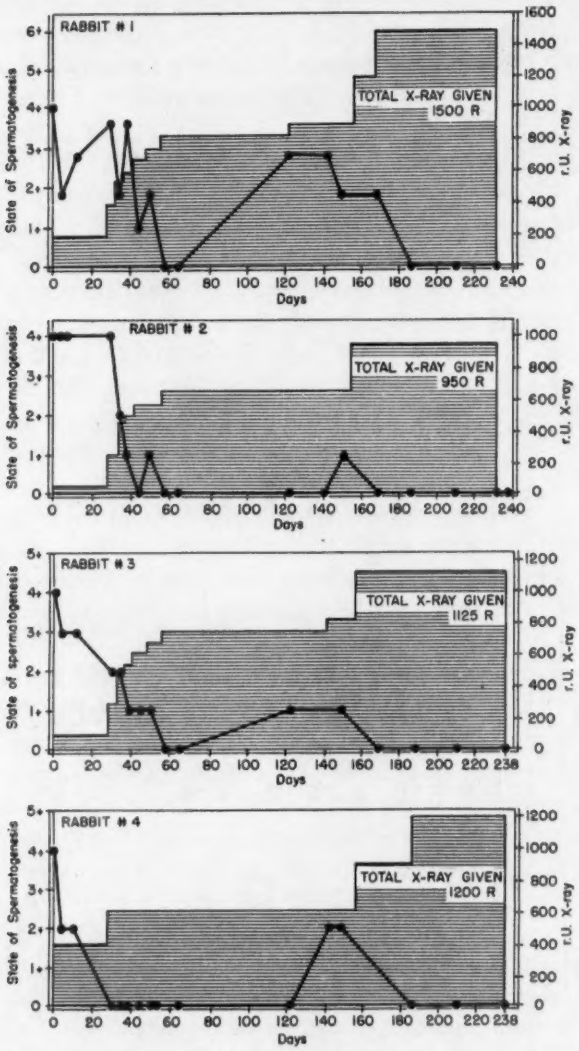

Fig. 2.—Detail diagrams of studies of roentgen ray irradiation and spermatogenesis.

6. Wigoder, S. B.: The Effect of X-Ray on the Testes, Brit. J. Radiol. **2**: 213-221 (May) 1929.

7. Momigliano, E., and Essenberg, J. M.: Regenerative Processes Induced by Gonadotropic Hormones in Irradiated Testes of the Albino Rat, Radiology **42**: 273-282 (March) 1944.

It has further been reported that 12 per cent of rats given 800 r to the testes in one treatment show complete sterilization.[8] Gonads of sexually mature domestic fowl require 1,276 r for initial injury and 2,400 to 2,800 r for total destruction of seminiferous epithelium.[9] These observations are summarized in table 2, with observations in respect to effects of roentgen rays on the rabbits' testes.

BIOLOGIC STUDIES ON THE IRRADIATED ANIMALS

Five adult white male rabbits from the same litter were given respectively 300, 600, 900, 1,200 and 1,500 r to the testes, with the same irradiation factors as in the previous experiment. A sixth rabbit was used as a control. After three months' observation each of these rabbits was placed with a female rabbit to see whether pregnancy ensued. The control rabbit and the rabbits that received 300, 600 and 900 r respectively successfully impregnated a female, with a resulting litter of

TABLE 2.—*Amount of Roentgen Ray Therapy Necessary to Depress, Temporarily Arrest or Stop Spermatogenesis*

Animal Tested (Author)	Dosage (r) Necessary to Depress Spermatogenesis	Dosage (r) Necessary to Produce Temporary Arrest of Spermatogenesis	Dosage (r) Necessary to Produce Sterility
Rabbit (Callaway, Moseley and Barefoot)	300 to 400	600 to 850	950 to 1,500
Mice (Snell [4])	.....	600	800 to 1,600
Rat (Wigoder [6])	.....	750	.....
Guinea pig (Strandskov [4b])	.....	422 to 864	.....
Albino rats (Momigliano [7])	.....	800	1,000 to 1,200
Domestic fowl (Essenberg and Karrasch [9])	1,276	.....	2,400 to 2,800

rabbits in each instance. The rabbits that had received 1,200 and 1,500 r respectively did not impregnate the female. Histologic study of the testes of these irradiated rabbits, killed after mating, showed that no arrest in spermatogenesis could be demonstrated on any of the testes of rabbits that received less than 1,200 r.

EFFECT OF IRRADIATION ON HUMAN TESTICLES

A 65 year old Negro man with carcinoma of the prostate gland was used for studies on irradiation. His scrotum was carefully shielded with lead, and 300 r was directed to the upper pole of the left testicle, 600 r to the lower pole of the right testicle, and 900 r to the upper pole of the right testicle. The lower pole of the left testicle was not irradiated

8. Hertwig, P.: Die Regeneration des Samenepithels der Maus nach Röntgensbestrahlung, unter besonderer Berücksichtigung der Spermatogonien, Arch. f. exper. Zellforsch. **22**:68-73, 1938.

9. Essenberg, J. M., and Karrasch, R. J.: An Experimental Study of the Effect of Roentgen Rays on the Gonads of the Sexually Mature Domestic Fowl, Radiology **39**:238-365 (March) 1940.

and was used as a control. In all instances the irradiation was filtered through 1 mm. of aluminum with a formula of 85 kilovolts and 5 milliamperes at a distance of 10 inches.

Three weeks later he was admitted to the hospital and a bilateral orchiectomy was performed. Both testes were obtained for histologic study, and sections were obtained from upper and lower poles of both testes.

In all of the microscopic sections there was atrophy of the seminiferous epithelium with no active spermatogenesis. There were, however, no discernible effects on the interstitial tissue from roentgen ray therapy in any of the sections.[10]

The second patient studied, a 51 year old Negro man with carcinoma of the prostate, was given roentgen ray therapy directly to the testes, with a formula of 85 kilovolts and 5 milliamperes with an aluminum filter of 1 mm. at 10 inches (25.4 cm.). The upper pole of the right testis was used as a control, and the lower pole of the right testis was given 300 r, with the rest of the testis carefully screened to prevent back scatter. The left testis was shielded in the same manner and with the same formula was given 600 r to the upper pole and 900 r to the lower pole. Four weeks later a bilateral orchiectomy was performed and the testes were studied histologically.

Careful histologic study revealed some generalized atrophy and scarring of the tubules thought to be due to senile changes. There were some cytoplasmic edema and minimal degenerative changes in certain of the seminiferous cells in the three poles that received irradiation. In these areas there was a lack of clarity in the nuclear structure. However, there was no suppression of spermatogenesis in any of the sections. The poles which received 300, 600 or 900 r showed as much active spermatogenesis as did the control area. There were no vascular changes in any of the sections.[10]

Admittedly, the first patient was a poor subject for such a study because of the lack of active spermatogenesis. It is suggested, however, that patients with carcinoma of the prostate gland who will require an orchiectomy are a source from which material may be obtained for evaluation of the effect of roentgen rays on the male gonads. We are now attempting to further this investigation with additional patients under study. When such patients exhibit active spermatogenesis and are studied in statistically significant numbers, one should be able to settle the problem of the effect of roentgen rays on human testes.

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10. The histologic sections were studied in conjunction with Dr. E. C. Hamblen, Dr. Clarence Davis, and Dr. C. J. Pattee of the Division of Endocrinology and Dr. Cyrus Erickson, Dr. Thomas Lide, Dr. Lalla Iverson and Dr. J. T. Cuttino of the Division of Pathology.

COMMENT

Wigoder [6] stated the belief that there is no correlation between different species of animals in regard to their tolerance to exposure of the gonads to roentgen rays. The tolerance of testes of rats, mice, rabbits and guinea pigs roughly approximates the tolerance of human ovaries. It seems possible that human testes might fall into this same range of sensitivity to roentgen ray irradiation.

As a conservative estimate, it has been stated that human ovaries, and perhaps testes, may be directly exposed to as much as 150 r without injury.[2a] Since, according to our studies, only 0.034 r would be expected to reach the gonadal region with each exposure of 100 r to the face, a dosage many times greater than any dosage ever used therapeutically would be required to produce theoretic damage to the gonads, even when the gonadal region is not shielded.

TABLE 3.—*Tolerance of Human Ovaries to Roentgen Rays*

Dosage (r) Producing No Injury (Author)	Dosage (r) Producing Temporary Sterility (Authors)	Dosage (r) Necessary to Produce Permanent Sterility (Authors)
150 (Westing)	360 to 510 (Westing) (Harris)	625 to 720 (Mayer and his associates) (Peck and his associates)

SUMMARY

The amount of scattered irradiation which may reach the gonadal region of patients receiving low voltage roentgen ray therapy to the face has been estimated as negligible so far as approaching the dosage which might produce injury to the gonadal tissues is concerned. A method for studying the effects of direct roentgen ray irradiation on the spermatogenesis of rabbits is described. Three hundred to 400 r are necessary to produce a suppression of spermatogenesis, 600 to 650 are necessary to produce a temporary arrest in spermatogenesis, and 950 to 1,500 r are required to produce a permanent arrest of spermatogenesis. Biologic studies demonstrated that rabbits that received 300, 600 or 900 r to the testes successfully impregnated female rabbits three months after irradiation, while rabbits that received 1,200 or 1,500 r were presumed to be sterile as a result of the roentgen ray irradiation. The testes of 2 patients with carcinoma of the prostate gland were given direct roentgen ray irradiation and subsequently were studied histologically after bilateral orchiectomy. No apparent arrest of spermatogenesis was produced by 300, 600 or 900 r. of roentgen ray irradiation.

MYCOSIS FUNGOIDES

Benign and Malignant Reticulum Cell Dysplasia

L. H. WINER, M.D.
BEVERLY HILLS, CALIF.

MYCOSIS fungoides has always been a subject for debate. Many investigators consider it neither a clinical nor a histologic entity. Therefore, they have placed it in the inclusive group of lymphoblastomas. Further support for this is the fact that mycosis fungoides may simulate other diseases of this group.

The histologic structure in the clinical picture of mycosis fungoides may be granulomatous, reticuloendotheliomatous or reticulosarcomatous. The reticulum of the skin is considered by many to be the site of origin. Some have thought that the perithelium, endothelium, adventitial or periadventitial histiocytes of the blood vessels in the cutis or the fixed connective tissue cells and fibroblasts were the matrix. The widespread character of the reticulum accounts for the generalized reaction, which is a constant feature of the disease.

The variable histologic appearance of mycosis fungoides is based on the many potentialities of differentiation of the reticulum cell. Scott and Robb-Smith,[1] on the basis of lymph node studies in reticulum cell sarcoma, classified five types of malignant reticulum cells: undifferentiated, differentiated to histioid cells, differentiated to hemic cells, mixed or polymorphic cells and differentiated to sinus lining cells. Furth[2] stated that most human neoplasms consisting of histiocytes were described under the term reticulum sarcoma. In mycosis fungoides the reticulum cells can form histiocytes, plasmacytes, fibroblasts and neoplastic reticulum or sarcoma cells. It is a transformation of one cell type into another rather than a neoplastic invasion. For this reason several investigators have considered mycosis fungoides as a step in dedifferentiation in the return of dermal tissue to an embryonal state.

Read at the Sixty-Sixth Annual Meeting of the American Dermatological Association, Inc., Hot Springs, Va., June 10, 1946.

From the Division of Dermatology, University of Minnesota, and the Division of Dermatology, Minneapolis General Hospital.

1. Scott, R. B., and Robb-Smith, A. H. T.: Histiocytic Medullary Reticulo-Endotheliosis, Lancet **2**:194-198, 1939.

2. Furth, J.: A Neoplasm of Monocytes of Mice and Its Relation to Similar Neoplasms of Man, J. Exper. Med. **69**:13-29, 1939.

Mycosis fungoides has two definite histologic divisions, one in the premycotic stage and the other in the tumor stage. The histologic study of the premycotic stage shows slight epidermal changes of liquefaction necroses of the basal cells and intraepidermal microabscesses of Pautrier, consisting of nests of monoyctes. In the cutis are the constant diagnostic polymorphous cellular conglomerations, consisting of lymphocytes, polymorphonuclear neutrophils, eosinophils, plasma cells, connective tissue cells, phagocytic histiocytes, nests of reticuloendothelial cells, pyknotic nuclei and fragmenting nuclei. The latter nuclear changes are due to the intense liquefaction necrosis, which gives a washed-out appearance to the cytoplasm of the proliferating cutis cells and is a characteristic of this stage of mycosis fungoides. In this phase, Gans,[3] Ormsby and Montgomery [4] and McCafferty and Machachek [5] stressed the pyknotic nuclei, karyorrhexis and phagocytosis of pigmented granular elements of debris. Jaffee [6] emphasized the richness of the eosinophilic leukocytes in this phase. Zoon [7] stated that the polymorphous image is so typical that it is impossible not to recognize the disease. Hematologists would classify this stage of mycosis fungoides as a complex reticulum cell proliferation, because of its polycellular nature.

In the tumor stage the histologic structure assumes a simple monomorphous pattern, with the cells in the cutis appearing more uniform. Nests of mitotic reticulum cells are evident. The cells appear to be joined by the reticulum fibers. In this stage the picture is that of a reticulum cell sarcoma. The characteristic reticulum cell, called the "mycotic cell," is most easily seen in this stage, being characterized by delicate cytoplasm and a large, round or oval nucleus. This cell is vulnerable and fades as though washed away.

This great vulnerability of the cells explains the clinical phenomenon of rapid spontaneous regression of the lesions of mycosis fungoides. Lapiere [8] and Margarot, Rimbaud and Ravoire [9] stated the belief that

3. Gans, L.: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, vol. 1, pp. 565-575.

4. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 6, Philadelphia, Lea & Febiger, 1943, p. 818.

5. McCafferty, L. K., and Machachek, G. H.: Lymphoblastoma: A Report of Two Cases, Arch. Dermat. & Syph. **21**:595-614 (April) 1930.

6. Jaffee, R. H., in Downey, H.: Handbook of Hematology, New York, Paul B. Hoeber, Inc., 1939, vol. 2, pp. 1105-1107.

7. Zoon, J. J.: Notes diagnostiques et therapeutiques au sujet du mycosis fongoïde, Bull. Soc. franç. de dermat. et syph. (Reunion dermat., Strasbourg) **44**:1282-1290, 1937.

8. Lapiere, S.: Étude comparative du mycosis fongoïde et de la maladie de Hodgkin, Rev. belge sci. méd. **10**:159-171, 1938.

9. Margarot, J.; Rimbaud, P., and Ravoire, J.: Quelques aspects cliniques et histo-pathologiques des hématodermies à forme tumorale, Montpellier méd. **15**: 211-228, 1939.

these cells originate from the histiocytes of perivascular tissue. In these cells the cytoplasm becomes enlarged and more granular, while the chromatin in the nucleus becomes irregular. Thus one can reconcile the frequent observation of phagocytic cells together with plasma cells, the latter of which are considered maturer forms of the histiocytes. The presence of reticulum mitotic figures indicates another of the multiphasic possibilities of reticulum proliferation. This characteristic has caused confusion and has resulted in the gross grouping of lymphoblastoma rather than in the classification of the several types of reticulum proliferation. Therefore, Fraser [10] and Wile and Styles [11] considered a mutation of clinical mycosis fungoides responsible for the cases which were observed at autopsy to be lymphosarcoma. Pardee and Zeit [12] reported a case in which mycosis fungoides became lymphatic leukemia just before death. Symmers [13] also reported a case of leukosarcoma in which a leukemic blood picture developed three weeks before death. Fraser's [14] case of premycotic fungoides was similar and two years later became "lymphatic leukemia." Montgomery and Watkins [15] reported cases of patients who clinically had lesions of mycosis fungoides, but the disease terminated in monocytic leukemia. Robb-Smith [16] stated that changes in the circulating blood are epiphenomena in reticuloses. Although several have expressed the belief that there was a transition of mycosis fungoides to Hodgkin's disease and to lymphosarcoma and have described it, there is no definite method of predicting this mutation.

REPORT OF CASES

CASE 1.—B. P., a white woman aged 55, was admitted to Minneapolis General Hospital March 19, 1940, complaining of a large ulcer of the left leg of fifteen months' duration. The ulcer was 14.5 by 9.5 cm. and extended into the muscles of the calf to a depth of 2.5 cm. The base exuded a sanguinopurulent discharge which had a foul odor. From several specimens for biopsy only a chronic suppurative inflammatory reaction was indicated. The ulcer was thought to be due to old deep thrombophlebitis, since there was a history of phlebitis following parturition thirty-two years previously.

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10. Fraser, J. F.: Mycosis Fungoides, J. Cutan. Dis. **35**:793, 1917.

11. Wile, U. J., and Styles, F., Jr.: Clinical Mutations in Lymphoblastomas, J. A. M. A. **104**:532-537 (Feb. 16) 1935.

12. Pardee, L. C., and Zeit, F. R.: Mycosis Fungoides, J. Cutan. Dis. **29**:7-19, 1911.

13. Symmers, D.: The Association of Certain Cutaneous Lesions with Diseases of the Hemopoietic System, J. Cutan. Dis. **37**:1-15, 1919.

14. Fraser, J. F.: Mycosis Fungoides: Its Relation to Leukemia and Lymphosarcoma, Arch. Dermat. & Syph. **12**:814-828 (Dec.) 1925.

15. Montgomery, H., and Watkins, C. H.: Exfoliative Dermatitis as a Manifestation of Monocytic Leukemia (Schilling), Minnesota Med. **21**:636-641, 1938.

16. Robb-Smith, A. H. T.: The Reticular Tissue and the Skin, Brit. J. Dermat. **56**:151-177, 1944.

Because of the patient's toxic state and septic temperature, ranging from 102 to 105 F., her left leg had to be amputated. The stump healed by primary intention, and she was discharged from the hospital. She was readmitted April 28, 1941 because of seropurulent drainage from a subepidermal nodule of the right thigh, from a biopsy of which a diagnosis of mycosis fungoides was made. The nodule was treated with 1,400 r (unfiltered) in split doses, which resulted in resolution and healing. New nodules subsequently appeared and became ulcerated. These nodules also involved the left thigh and the area of the amputation stump, making it impossible for the patient to wear an artificial limb.

She was again readmitted to the dermatologic service on Oct. 16, 1942 because of recurrence of cutaneous ulcers, and on Jan. 20, 1943, there was a sudden elevation of temperature to 104 F. and pain in the right side of the chest, associated with a cough. There were decreased breath sounds and dulness to per-

Fig. 1 (case 1).—Ulcer of the leg in a *d'emblée* form of mycosis fungoides.

cussion in the lower part of the right side of the chest. A roentgenogram showed fluid in the base of the right side of the chest, with congestion and consolidation in that area, and a diagnosis of pneumonia of the lower lobe of the right lung was made. Pneumotyping showed a type XVII pneumococcus. After the administration of sulfathiazole the temperature returned to normal within three days. However, there were daily elevations of temperature to 100 F. A roentgenogram of the chest at this time showed a density in the right cardiophrenic angle and a rounded mass in the right side of the chest posteriorly. On February 24, a thoracentesis of the right pleural cavity was performed, which showed a cell count of 2,365 white cells per cubic millimeter, with 21 per cent neutrophils and 79 per cent mononuclear cells. Culture of this fluid did not produce organisms. High daily elevations of temperature recurred, and she became critically ill. She died on March 14.

An autopsy was performed, and the pathologic diagnosis was mycosis fungoides, with involvement of the skin, right lung, kidney and liver, and bronchopneumonia and pleural effusion of the right lung.

Comment.—The histologic section of the skin from the earliest ulcers showed a granulomatous process which consisted essentially of reticulum cells, histiocytes, plasma cells and fibroblastic proliferation. In some sections plasma cell nests were dense. Reticulum cells can proliferate to form plasma cells.

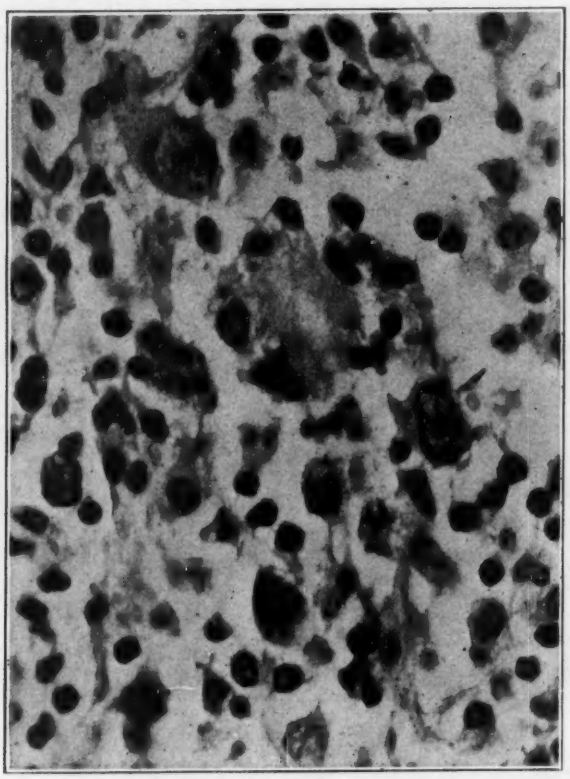

Fig. 2 (case 1).—Section of ulcer of figure 1, showing large histiocytes, plasma cells, lymphocytes and cell nests undergoing liquefaction necrosis. × 650.

This case was mycosis fungoides of the *d'emblée* type. The lymph nodes were not involved. The lesion of the lung was confusing, as it was first diagnosed as primary pneumonia. At autopsy the gross pulmonary tumor looked like a bronchiogenic carcinoma. Only on histologic section could the diagnosis of mycosis fungoides be made. Berman [17] collected 60 cases of mycosis fungoides in which there was visceral

17. Berman, L.: Pathologic Nature of Mycosis Fungoides with Report of a Case, Arch. Path. **29**:530-540 (April) 1940.

involvement. Werth [18] found 31 instances of pulmonary involvement and added 2 cases of his own. He stated that reports of pulmonic lesions of mycosis fungoides were uncommon because of physicians' failure to obtain roentgenograms of the chest. Werth described the lesion of mycosis fungoides of the chest, as shown roentgenographically, as marble-like but showing the clear apexes until late in the disease, which differentiates it from tuberculosis. However, atypical tuberculosis, miliary tuberculosis and miliary lupoid (Boeck's sarcoid) had to be considered and ruled out.

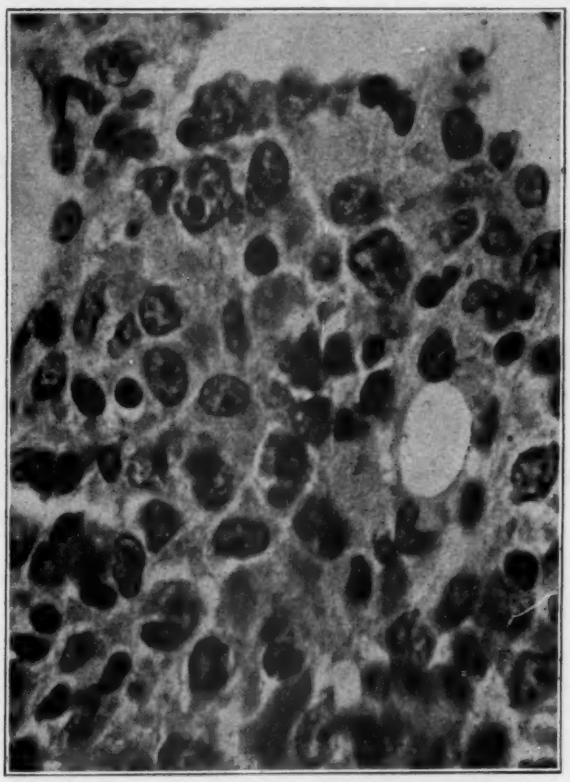

Fig. 3 (case 1).—Section of the ulcer of the leg in figure 1, showing numerous proliferating reticulum cells as well as karyorrhexis and pyknosis of nuclei. × 650.

Case 2.—A. L., a man aged 72 years, was admitted to the Minneapolis General Hospital on Sept. 21, 1943, complaining of itching of the legs and reddened areas on the back, of six months' duration. The itching became so severe that he was unable to sleep. Two months before admission, a "sore" developed on his back, and the sore had increased in size.

18. Werth, J.: Ueber Lungenröntgenbefunde bei Mycosis fungoides, Arch. f. Dermat. u. Syph. **181**:299-314, 1940.

Observations of physical abnormalities were limited to the skin, which showed patchy areas of pinkish red circinate weeping lesions over the sacrum. An area 2 by 2 cm. and elevated 0.5 cm. was noted over the left lower quadrant of the abdomen. Many scaly indurated lesions were scattered over the body. There were numerous excoriations.

Histologic section of the skin from both the indurated areas of the abdomen and the eczematous areas over the sacrum showed pleomorphic cell nests of reticulum cells, lymphocytes, plasm cells, histiocytes and fibroblasts. Pyknosis and karyorrhexis were evident in the midst of the proliferating cells. The histologic diagnosis corroborated the clinical diagnosis of mycosis fungoides.

Fig. 4 (case 2).—Ulcerated tumor stage and horseshoe plaques of mycosis fungoides.

The patient was given roentgen therapy, 13 r of general radiation in each of eight treatments, to the front and back at 130 cm. distance, filtered with 0.25 mm. of copper and 1 mm. of aluminum at 130 peak kilovoltage and 5 milliamperes. After the eighth treatment the roentgen therapy had to be discontinued because of the pronounced reduction in the white blood cell count. He was discharged on November 4, but was readmitted March 28, 1944 because a tumor 10 by 15 cm. had developed over the sacrum. The inguinal lymph nodes were also noticeably enlarged. Biopsy specimens of skin, tumor and lymph nodes were taken. Histologically, the lymph node showed loss of normal architecture. The lymph follicles were replaced by reticulum cells, many showing various stages of mitosis. The

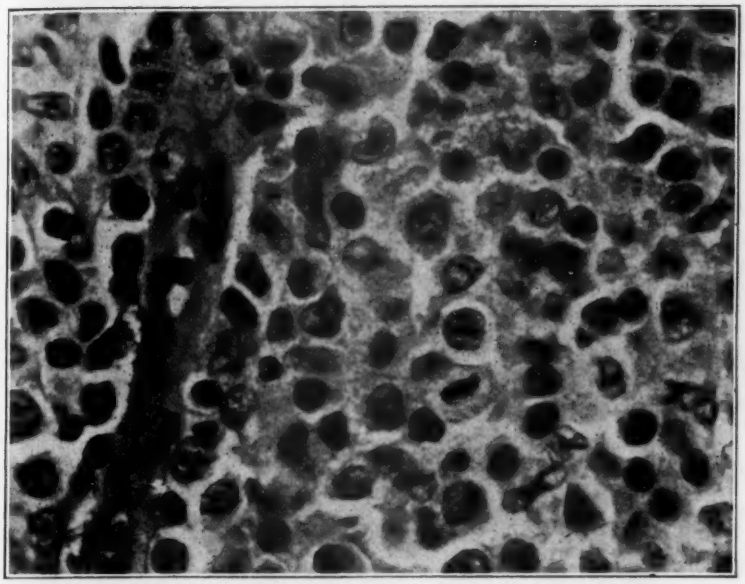

Fig. 5 (case 2).—Lymph node showing two mitotic figures and replacement of normal structure by proliferating reticulum.

Fig. 6 (case 3).—Diffuse alopecia in mycosis fungoides involving the scalp.

cutaneous sections showed replacement of the normal cutis by reticulum cell hyperplasia, and numerous mitotic figures were evident. The histologic structure had a striking monomorphous character, and the diagnosis of mycosis fungoides progressing to a reticulum cell sarcoma was made. The peripheral blood and bone marrow were normal. Roentgenograms of the stomach, lungs and heart showed nothing abnormal. The sacral tumor softened and ulcerated. The patient died on May 30. Permission for an autopsy could not be obtained.

Comment.—Clinically this patient had typical mycosis fungoides, in which severe itching preceded objective signs by six months and progressed from erythematous plaques (premycotic) to eczematous

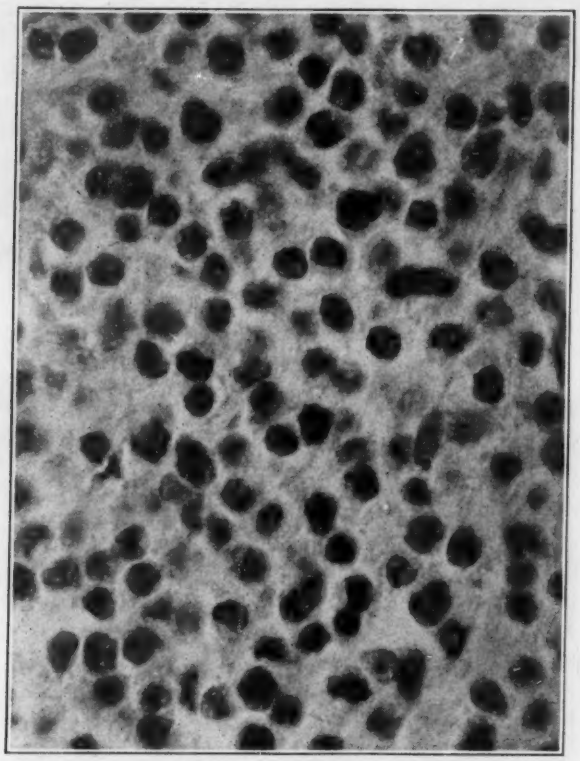

Fig. 7.—Four mitotic figures. × 650.

(mycotic) lesions, with indurated tumors, and finally to ulceration. Histologically, the early pleomorphic cellular infiltration and the late monomorphous cell proliferation were typical of mycosis fungoides. The reticulum cell sarcoma involved both skin and lymph nodes in this patient. Lymph node imprints were obtained and showed actively proliferating reticulum cells.

CASE 3.—E. A., a white woman aged 61 years, was admitted to the Minneapolis General Hospital Oct. 2, 1943, complaining of severe burning and itching of the skin, of one year's duration. At onset the eruption appeared as generalized

scattered large red macules which subsequently developed scales, then oozed and formed crusts. These crusted areas broke down and formed large painful chronic ulcers.

Physical examination revealed nothing unusual except for the skin, which was covered by numerous scaly and crusted plaques and ulcers. The eruption of the scalp was covered by grayish white firmly adherent scales and resulted in diffuse alopecia. There was pitting edema of the ankles.

Reactions to serologic tests of the blood were negative for syphilis. The hemoglobin was 54 per cent, the red cell count 2,770,000 and white cell count 7,600, with 66 per cent neutrophils, 14 per cent lymphocytes, 19 per cent monocytes and 1 per cent eosinophils. The platelet count was 310,000. The morphologic

Fig. 8.—Photomicrograph of lesion of mycosis fungoides. × 100.

study of the blood showed an average mean red cell diameter of 7.7 microns, with slight polychromasia, slight poikilocytosis and slight anisocytosis. Many of the red cells showed lipoid degeneration. The white cells appeared toxic. Some of the monocytic cells appeared to be monocytoid histiocytes. Examination of the urine revealed no abnormalities except for a faint trace of albumin. A roentgenogram of the chest showed thickening of the pleura of the wall of the right side of the chest.

Biopsy specimens of the ulcers and indurated areas of the skin were taken. Microscopic examination revealed that the cutis contained a pleomorphous cell infiltration, consisting of reticulum cells, fibroblasts, plasma cells, histiocytes and lymphocytes. Karyorrhexis was evident throughout the sections, as were numerous

phagocytic histiocytes. The histologic diagnosis of mycosis fungoides confirmed the clinical impression.

Roentgen rays were administered to the involved areas of the skin, and multiple small blood transfusions (200 to 300 cc. of citrated whole blood) were necessary to maintain the level of the hemoglobin. The skin improved appreciably for about six weeks, then there was general and gradual deterioration, and she died Feb. 27, 1944.

An autopsy was performed. Microscopic examination of a mesenteric lymph node showed reticular hyperplasia, but normal architecture. The spleen also showed reticular hyperplasia and an increase in the number of neutrophils and plasma cells. Some of the malpighian corpuscles were practically obliterated. The diagnosis was mycosis fungoides.

Comment.—The foregoing is a classic picture of mycosis fungoides, clinically and histologically. At autopsy the amount of gross pathologic changes present seemed insufficient to explain the severe toxic state of the patient. This can be accounted for by the tendency of mycosis fungoides to resolve itself and melt away. This phenomenon is also seen in the cases of mycosis fungoides which assume neoplastic characteristics, with involvement of regional glands and internal organs, and in which there is replacement of normal structures by neoplastic ones containing numerous mitotic figures. Cutaneous imprints and lymph node imprints were unsatisfactory, as they were made at autopsy and the cells had already undergone postmortem degeneration.

Case 4.—A. W., a white woman[19] aged 76, was admitted to the hospital on Aug. 14, 1945, complaining of an eruption, which began two years previously as generalized itching erythema and exfoliation. The erythema and exfoliation subsided after about one year and were followed by indurated plaques and tumors, some of which ulcerated and then later healed leaving hyperpigmented rings in the skin.

Examination revealed the skin of the trunk, face and extremities to be involved by numerous indurated dusky red plaques and tumors, some of which were ulcerated. The dorsa of the feet and the anterior surfaces of the legs and thighs had dark bluish red firm nonelevated nodules, which were not ulcerated and which the patient stated came on six weeks before admission. The latter lesions did not itch. There was pitting edema of the legs and ankles. The clinical diagnosis was mycosis fungoides and idiopathic hemorrhagic sarcoma of Kaposi.

A specimen was taken for biopsy from an ulcerating tumor on the right shoulder. Microscopic section of this tissue showed nests of actively proliferating large reticulum cells and phagocytic reticulum cells or histiocytes and a few plasma cells. Tissue imprints showed large mononuclear reticulum cells with oval nucleus and finely granular vacuolated cytoplasm. The nucleus consisted of lacy chromatin and contained three large nucleoli. The diagnosis from the section was mycosis fungoides.

A biopsy was made from one of the firm nodular lesions on the lower extremities. Microscopic sections of this lesion showed that the cutis contained great nests of proliferating fibroblasts, new blood vessel formations and large amounts of extravasated blood. Tissue imprints from this nodule showed only fibroblasts.

19. Permission to present this case was granted by Dr. S. Ayres Jr.

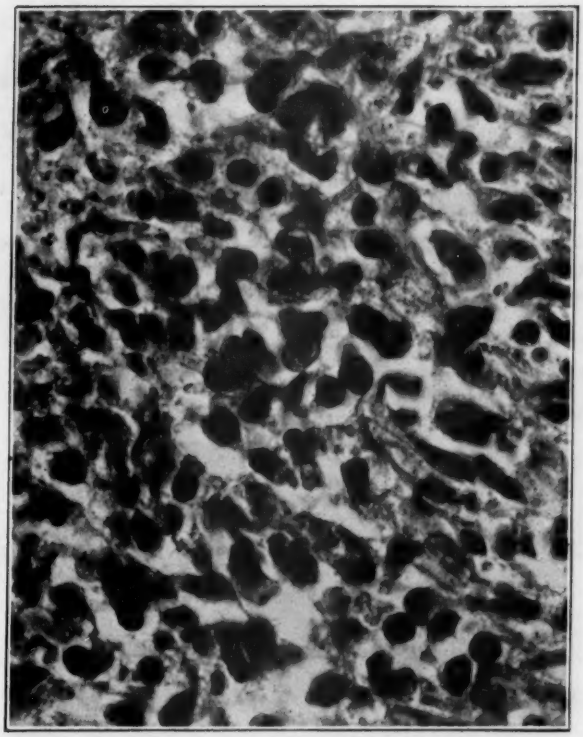

Fig. 9 (case 4).—Photomicrograph showing the phagocytic characteristics of the histiocytes. × 650.

Fig. 10 (case 4).—Photomicrograph of malignant reticulum cell from a cutaneous tumor imprint of mycosis fungoides. × 2100.

The histologic diagnosis of this nodule was idiopathic hemorrhagic sarcoma of Kaposi.

The patient was treated intensively with roentgen rays, subcutaneous and intravenous injections of antireticular cytotoxic serum (A. C. S.), repeated transfusions and intravenous injections of serum, all without altering the course of the disease, and she died Jan. 15, 1946. Permission for an autopsy was not granted.

It was observed in the final periods of the patient's illness that the cutaneous lesions began to regress and the skin looked closer to normal, but the patient's general condition became worse.

Comment.—From this case it is seen that both mycosis fungoides and idiopathic hemorrhagic sarcoma of Kaposi can exist in the same

Fig. 11.—Photomicrograph of a lesion of idiopathic hemorrhagic sarcoma of Kaposi in case 4, showing intense fibrosis. × 100.

patient, but their clinical course as well as histologic appearance differs and the types of cells seen on tissue imprints were not the same.

DIFFERENTIAL DIAGNOSIS

In the differential diagnosis Hodgkin's disease must be considered. Clinically Hodgkin's disease begins in the lymph nodes and secondarily involves the skin, with the exception of the rarely occurring primary Hodgkin disease of the skin. Mycosis fungoides, on the other hand, involves the skin first and the lymph nodes secondarily. Histologically,

in the tumor stage of Hodgkin's disease polymorphous cell structures are seen, whereas in the comparable tumor stage of mycosis fungoides cellular masses are monomorphous. Necrosis occurs in both, but in Hodgkin's disease there is a more fibrinoid caseation necrosis, whereas in mycosis fungoides it is a liquefaction necrosis. The Sternberg-Reed giant cells are seen in Hodgkin's disease, but giant cells of this type are rare in mycosis fungoides.

Civatte,[20] MacCormac,[21] Durand, Cottenot and Mamou,[22] Lever [23] and others have noted similarity between mycosis fungoides and Hodg-

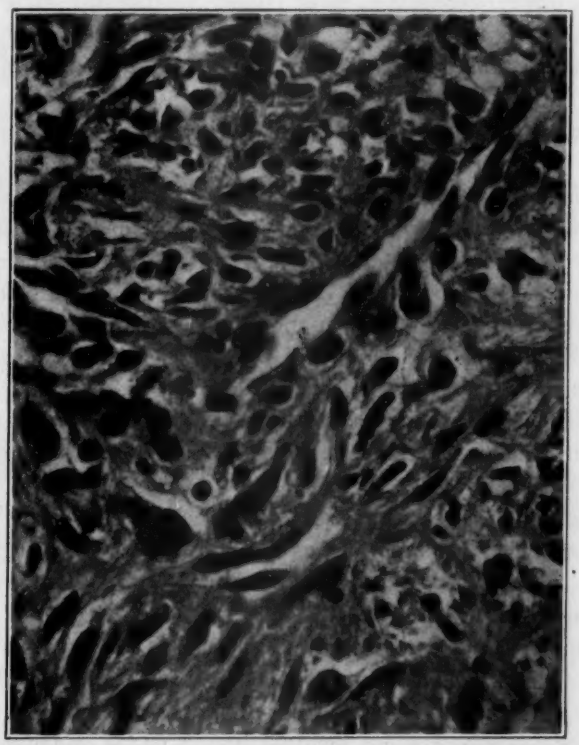

Fig. 12.—Same as figure 11. Photomicrograph showing immature as well as mature fibroblasts, new vessel formations and histiocytic reticulum cell. × 650.

20. Civatte, A., in Darier, J.: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, vol. 1, p. 266; in discussion on Touraine, A.: Lepagnole et Neret M. reticulo-endotheliose paremycosique, Bull. Soc. franç. de dermat. et syph. **45**:1806-1807, 1938.

21. MacCormac, H.: Mycosis Fungoides Treated by Malaria Terminating in Hodgkin's Disease. Brit. M. J. **2**:645-646, 1941.

22. Durand, H.; Cottenot, P., and Mamou, H.: Les formes cutanées ulcereuses de la maladie de Hodgkin, Presse méd. **46**:1723-1725, 1938.

23. Lever, W. F., in discussion on Mycosis Fungoides; Aplastic Anemia, Cabot Case 27352, New England J. Med. **225**:341-343. 1941.

kin's disease. This resemblance is evident because the parent tissue of the two diseases is the reticuloendothelial system. However, the preponderance of the malignant reticulum cells with the large single nucleoli is characteristic of Hodgkin's disease, whereas in mycosis fungoides this type of cell was not so numerous. In the tissue the large histiocytic cells containing a round nucleus with multiple small nucleoli and large irregular cytoplasm were most evident. Phagocytosis, karyorrhexis and pyknosis are features of mycosis fungoides which are not seen in Hodgkin's disease. However, immature reticulum cells are also seen in mycosis fungoides as in Hodgkin's disease. In some of the cases (case 2), in the terminal phases, these diseases look alike histologically, because the parent tissue is the same and because of repeated and continuous insults on this tissue it responds in both diseases ultimately in the same manner to form reticulum cell sarcoma.

Also to be considered in the differential diagnosis are leukemia cutis, multiple idiopathic hemorrhagic sarcoma (Kaposi), melanoma, dermatofibrosarcoma, lymphosarcoma and metastatic carcinoma.

In leukemia cutis characteristic features are the leonine face, purpuric subcutaneous hemorrhages and early involvement of the blood stream. Histologic characteristics are the dense cellular infiltrations, without any mitotic figures and the zone of normal connective tissue between the epidermis and the proliferating cellular infiltrations. Multiple idiopathic hemorrhagic sarcoma has proliferating fibroblastic structures together with massive extravasations of blood into the nests of proliferating fibroblasts.

Melanoma is difficult to diagnose when melanin is absent. However, the nuclei of melanoma cells are, as a rule, much smaller in relation to their cytoplasm than are those of the histiocytic reticulum cells seen in mycosis fungoides.

Dermatofibrosarcoma, although numerous mitotic figures are present, is seen to consist of intertwining bundles of fibrous connective tissue, and at all times it is monomorphous in its cellular character.

Small cell lymphosarcoma involves lymph nodes and mucous membranes primarily and is characterized by a more highly differentiated type of cell.

Metastatic carcinoma can be seen to lie in the sinusoids of the lymph nodes, compressing the medullary tissue.

SUMMARY AND CONCLUSIONS

Mycosis fungoides is a disease in which tumors develop which are similar to those in chronic aleukemic or leukemic monocytic leukemia. As in lymphatic or myelogenous leukemia, the cutaneous tumors are manifestations of the underlying disease.

In the disease called mycosis fungoides, the reticulum cells may differentiate into diverse types on one hand and undergo liquefaction necrosis or become malignant on the other.

Hodgkin's disease at some stages may resemble mycosis fungoides because of their common matrix, but Hodgkin's disease is at all times a malignant reticulum cell sarcoma and ends fatally.

In 1 patient with mycosis fungoides there was an associated hemorrhagic sarcoma of Kaposi, but these were two diseases entirely independent of each other.

Dr. Emil Schleicher, hematologist of Minneapolis General Hospital, assisted in the staining and diagnosing of the cutaneous imprints, and the photomicrography was done by Henry Morris, University of Minnesota.

416 North Bedford Drive.

ABSTRACT OF DISCUSSION

Dr. Samuel E. Sweitzer, Minneapolis: A discusser should have something extra to offer or have something to criticize before he starts to discuss. I have little extra to offer, and I have nothing in particular to criticize. I should like to make some observations, however, in view of the fact that Dr. Winer and I wrote a paper on Hodgkin's disease which I presented two years ago, and in looking up the literature, we noted a great deal of confusion about these two diseases. Many cases were reported as beginning mycosis fungoides and ending in Hodgkin's disease, and vice versa. So, there has been some tendency to lump these diseases into generic terms of the lymphoblastomas, on the basis that they are all varieties of the same condition.

It might be possible that this is true. However, at the University of Minnesota I and, I think, my associates are rather inclined to keep these apart until we know more about them. These cases that Dr. Winer reported today, or most of them, were from my clinic, and I think that none of you would have difficulty in making a diagnosis of mycosis fungoides. They showed typical textbook pictures. Most of us believe that it is better to keep the clinical and histologic distinctions separate, if possible, and to continue to make use of the old terms, such as Hodgkin's disease and mycosis fungoides, instead of lymphoblastoma, until we know more about the cause.

One other thought came to me as to the cause of these diseases, and digression for a moment might illustrate what I mean. Dr. Green and Dr. Bittner, of the University of Minnesota, working on the causation of mouse carcinoma—you may have heard of their observations—bred some mice, and carcinoma developed in practically all of them. But if the offspring are taken away before they have nursed over twenty-four hours, carcinoma will not develop in them. Also, if the milk is centrifuged rapidly, substances from a certain stratum of that centrifuged material can be injected into mice and so induce carcinoma in them. Dr. Green is convinced that carcinoma is due to a virus. Of course, he is a specialist in viruses, and maybe he is prejudiced.

The thought came to me that there is at least a slight possibility that the diseases, like mycosis fungoides, in which these tumors of the lymphoblastoma group are formed, might be due to a virus, because a virus can cause a wart, as Dr. Wile so well figured out many years ago, and many other diseases are caused by viruses, so that there is a possibility that a virus might cause these peculiar tumors that we group under lymphoblastomas.

DR. C. GUY LANE, Boston: I was much interested in Dr. Winer's paper because at the Massachusetts General Hospital I have followed most of the cases of mycosis fungoides for the last twenty-five years, and my colleagues and I are now reviewing some 80 cases which were recorded there over a longer period than that. We have not gone far enough to develop real statistics, but I have acquired certain impressions in that time with regard to these cases.

At one time, not so long ago, we observed that in about 20 per cent of the patients there had developed terminal changes in the blood, and in 2 of them they developed with the most rapid lymphatic leukemia that I have ever seen. In 2 other patients there developed severe terminal edema of the upper part of the body. Both of these experienced changes following the so-called spray treatment of radiation.

We have had 2 or 3 cases in which the patient was given a diagnosis in the beginning of psoriasis, and in 2 of them, as the eruption cleared up with roentgen rays, it was observed that another eruption persisted which was later determined to be psoriasis. As Dr. Winer suggested, 1 case was reported in which a rapid and terminal Kaposi sarcoma developed, a case which was reported by Dr. Greenwood and me.

In 1 other case, which I have mentioned before, the patient experienced a striking change for the better, which occurred after a streptococcic infection. This patient was seen by me in what I thought was a terminal phase. An abscess was operated on, and pure streptococcus was observed. When I saw him two months later he was 75 per cent improved, but we were not able to continue with any streptococcic vaccine developed from his culture, and he died a couple of years later.

I suppose that it is too late now to change the term mycosis fungoides to get away from the general medical conception of mycosis as a ringworm infection. I suppose that it is too late to change to granuloma fungoides or even to speak of lymphoblastoma in the fungoid stage, but it is too bad to have the disease confused with mycotic infections.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: Dr. Winer has given a thorough review of the subject of mycosis fungoides. He will recall, however, some of the cases of mycosis fungoides which hemocytologists at the University of Minnesota have diagnosed as reticuloendotheliosis. I believe that the term lymphoblastoma should be preserved and that one cannot predict from the clinical appearance of mycosis fungoides whether it is that disease and is going to remain as such or whether it is going to eventuate in one of the other forms of lymphoblastoma. Some cases of mycosis fungoides remain as such, without involvement of the internal or blood-forming organs, for twenty or more years. I saw a case which clinically and histologically was mycosis fungoides of the skin, but with lymphatic leukemia in the blood and lymphosarcoma in the lymph nodes. Mycosis fungoides may also start as generalized dermatitis or erythroderma, simulating atopic dermatitis, and clear up with treatment with simple ointments only to recur after a period of months or years, with typical lesions of mycosis fungoides. It is often necessary, I believe, to make use of all diagnostic procedures, including biopsies of the skin, lymph node and, at times, bone marrow and hemocytologic studies, together with observation of the patient over a varying period before one can arrive at a diagnosis of mycosis fungoides or any other type of lymphoblastoma.

DR. HARTHER L. KEIM, Detroit: Dr. Lane has expressed some of my ideas, but, on the contrary, I do feel it is not too late. In fact, I believe that it is past time to start to do something about the term mycosis fungoides. It does not appear anywhere except in dermatologic literature, and I think that we, as derma-

tologists, are to be condemned for continuing to use it, at least without some qualifying adjective. It has been well over a hundred years since the name mycosis fungoides has been applied to this clinical syndrome.

We know, of course, that it is not mycotic, and at the present time, with roentgen ray therapy being used extensively in its management, few of the lesions fungate. It is my belief that it should be included in the group of lymphoblastomas, and until some appropriate terminology has been found we should at least refer to it as "so-called mycosis fungoides." Pathologically it is generally accepted that this syndrome is a cutaneous expression of at least three different diseases of the lymph node system, namely, Hodgkin's disease, a variety of round cell sarcoma arising from the connective tissue reticulum of the lymph nodes or elsewhere and lymphosarcoma originating in the lymphoid cells of the lymph nodes or other lymphoid structures. In short, mycosis fungoides as an independent disease does not exist.

Dr. Fred W. Weidman, Philadelphia: I did not hear Dr. Winer say anything about the eosinophilia that is frequently seen in granuloma fungoides and I am pleased indeed that Dr. Montgomery said what he did about the irregularity in the various features that can occur in mycosis fungoides because it repeats what I tried to indicate this morning about a possible explanation of the extremely varied clinical features which have been reported in reputed cases of eosinophilic granuloma (to be reported in the Archives of Dermatology and Syphilology). In fact, I met great difficulty in diagnosing the case of Dr. Miale which was included in my series because it resembled mycosis fungoides so much, and it was only on the basis of the tremendous number of eosinophils that I (at least tentatively) included his case. I am sure that if the eosinophils had been present in smaller numbers, I would have diagnosed it as a typical example of mycosis fungoides.

Irregularities also occur in that other reticuloendothelial disease, namely, Hodgkin's disease. My study of eosinophilic granuloma indicated the necessity for studying the fat content in future investigations of both Hodgkin's disease and mycosis fungoides. As a corollary to that, with the difference that there is in the prognosis of eosinophilic granuloma and mycosis fungoides, it might be that the fat content determines that difference. After that, the introduction of fat into the picture, whether locally or systemically, might modify the course of mycosis fungoides.

Impression preparations should be routinely made in future cases of eosinophilic granuloma, as I stated this morning. For a long time they have been routine in the technic of hematologists. Such studies of bone marrow are necessary because in histologic sections there is shrinkage due to the fixative and alterations in the finer details of characteristics by which such cells as premyelocytes and monocytes may be distinguished. I have never seen in a histologic section, no matter how well it might be stained, any granules that were significant for the monocytes, and it is only by making impression preparations that one can get those ultimate and finest details which are necessary in thoroughly analyzing the hematopoiesis of so-called lymphoblastomas.

Dr. Louis H. Winer, Minneapolis: I agree with the constructive criticisms of the terminology.

As regards the leukemic picture that Dr. Lane mentioned, Robb-Smith, in his paper on reticulum, mentioned the fact that in reticulum diseases leukemic pictures are epiphenomena. We also know from clinical experience at the University of Minnesota that patients with diabetic coma may have a white cell count of lymphocytes as high as 300,000. With the diabetic coma under control, the blood picture

returns to normal within twenty-four hours. Why these patients with coma present this picture I do not know, but, anyway, a high white blood cell count is simply a pouring out of cells into the blood stream, and it can also occur in mycosis fungoides.

Dr. Montgomery and Dr. Burkhart discussed mycosis fungoides with a monocytic leukemia picture. The monocyte in the blood is the counterpart of the reticulum cell in the tissue. A characteristic of the reticulum cell is that it can undergo liquefaction necrosis.

Dr. Weidman mentioned the eosinophilia. Jaffee, in "The Handbook of Hematology," stated that mycosis fungoides is characterized by its heavy eosinophilia. I am appreciative of Dr. Weidman's bringing out that prognostic point, because it seems that the more malignant the mycosis fungoides the fewer the number of eosinophils.

LIPSTICK CHEILITIS

A Common Dermatosis: Report of Thirty-Two Cases

SAMUEL J. ZAKON, M.D.

AARON L. GOLDBERG, M.D.

AND

JULIUS B. KAHN, B.S.

CHICAGO

CHEILITIS is one of the most commonly seen dermatoses in clinical practice. Among the most frequent causes of this disease in women is the dye used to impart lasting qualities to indelible lipsticks. This dye is dibromfluorescein, tribromfluorescein or tetrabromfluorescein.

Many other causative agents of cheilitis have been reported in the literature. Various authors have reported cases of cheilitis due to the following: actinic or chemically active rays of sunlight,[1] cold urticaria,[2] carmine and anilin dyes in liquid rouge,[3] trout,[4] lipstick,[5] methyl heptine carbonate in the perfume of lipstick,[6] dental plates ("hecolite"),[7] eosin dye in lipstick,[8] denture creams containing oil of anise,[9] lipstick in which local factors play a part,[10] mouth washes and cigaret holders,[11]

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derivatives of bromfluorescein (with photosensitization a factor to be considered), a husband's moustache wax, amalgam fillings for teeth, toothpaste and a preparation for gums in pyorrhea ("oryl") containing oil of cinnamon and oil of cloves, orange juice and tomato juice,[12] tetrabromfluorescein dye in lipstick,[13] lipstick and an associated sensitivity,[14] nail polish,[15] certain toothpaste ("ipana" and "kolynos"),[16] hexylresorcinol in lozenges and in toothpaste,[17] lipstick in metallic containers,[18] Italian reed,[19] volatile oil such as oil of orange in bubble gum,[20] tetrabromfluorescein dye sensitivity (purification into five residues resulted in negative responses to the fifth residue),[21] again eosin dye plus photosensitization, mango rinds, tincture of krameria,[22] sage tea, strong artificial lights such as carbon arc lights,[23] and liquid lip rouge.[24]

Since bromfluorescein dyes are more frequent offenders than any of the other aforementioned causes, the manufacture and the chemistry of indelible lipsticks will be discussed in this paper, and 32 cases of sensitivity to indelible lipstick dyes will be presented.

Since lipsticks are used today by more women than is any other cosmetic, it is now more important than ever that physicians be informed

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12. Sulzberger, M. B., and Goodman, J.: Acquired Specific Sensitivity to Simple Chemicals: Cheilitis with Special Reference to Sensitivity to Lipstick, Arch. Dermat. & Syph. **37**:597-615 (April) 1938.

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of their composition. For this reason we will review the composition of commercial lipsticks as well as the lipstick without indelible dyes used in the cases described in this paper.

A good lipstick is difficult to make, because to be acceptable to the modern woman it must meet all the following specifications: 1. It should apply easily and evenly. 2. It should not be too greasy. 3. It should not "bleed." 4. It should be of proper melting point, so that it will not melt or lose its shape in hot summer weather and, at the same time, soft enough to apply evenly during the cold of winter. 5. It should not "sweat." 6. It should not crumble or crack. 7. It should have an agreeable odor and taste. 8. The colors should be uniformly blended and ground into the wax and oil base.

Lipsticks consist of a wax, fat and oil base, into which are blended oil-soluble dyes and lake colors. All colors, whether dyes or lakes (pigments), must meet standards of chemical purity prescribed by the Federal Food and Drug Administration, and each batch must be certified by that agency as meeting those standards before it can legally be used by cosmetic manufacturers. The United States Government certifies only to the chemical standards of these colors but makes no attempt to consider their allergenic properties. Sensitivity to the lake colors is rare, but sensitivity to the dyes is more frequent than is commonly realized, as we indicate later.

The waxes generally used in lipsticks are beeswax, paraffin wax, ceresin (ozokerite), carnauba wax and spermaceti.

The fats most commonly used are theobroma oil (cocoa butter), benzoinated lard, cetyl alcohol, wool fat, hydrogenated vegetable oils, petrolatum and cholesterol absorption bases.

As solvents for the waxes and fats the following oils are most often used: mineral oil, soya bean oil, peanut oil and sesame oil. Castor oil and butyl stearate are also used to dissolve the indelible bromfluorescein.

To impart odor and taste an almost endless variety of natural and synthetic flower and essential oils is used.

The lipstick prescribed for the patients with whom we are concerned in this paper contained, in addition to the certified cosmetic lake colors, white petrolatum U. S. P., liquid petrolatum U. S. P., sun-bleached depollenized beeswax and theobroma oil U. S. P. None of the lipsticks successfully used by these patients contained perfume or any halogen derivative of fluorescein.[25]

25. The lipstick used in this series was supplied by Ar-Ex Cosmetics, Inc., Chicago and is available now as "Ar-Ex special formula" or "now-permanent" lipstick.

Patient	Case	Age, Years	Duration of Symptoms	Location of Lesions	Type of Lesions	Comments
D. F.	1	21	2 years	Lips	Fissure	Lips normal after using lipstick containing no indelible dye for 14 days
E. F.	2	28	12 years	Lips	Fissure, which bled at times	Lips normal after using lipstick containing no indelible dye 6 weeks
E. G.	3	40	2 weeks	Lips	Chapped, burning, itching, no fissures	Lips "perfect" after using lipstick with no indelible dye 3 weeks
H. K.	4	24	3 months	Lips	Fissure, cracks in corners	Lips normal after using lipstick with no indelible dye 10 days
R. L.	5	30	5 weeks	Lips	Fissures, painful	Lips completely healed after using lipstick with no indelible dye 3 weeks
E. L.	6	47	1 week	Lips	Fissures, edema, blisters	Lips normal; patient can use lipstick without indelible dye
S. L.	7	54	Several years since started to use lipstick	Lips	Fissures, burning edema	Lips normal for first time since lipstick was first used; patient uses lipstick with no indelible dye
M. M.	8	27	10-12 years—since started using lipstick	Lips	Fissures	After 14 days of use of lipstick containing no indelible dye lips normal
O. P.	9	21	1 year	Lips, mouth, neck and eyelids	Fissured lips, eruption on neck and eyelids	All fissures and eruption around neck and eyes cleared after using lipstick with no indelible dye 3 days
H. S.	10	26	2 months	Lips, both sides of face and chin	Lips fissured, red blotchy dermatitis on face	All symptoms completely disappeared after using lipstick containing no indelible dye for 5 days
L. W.	11	44	.....	Lips, chin	Fissures, lips and chin dry, cracking, irritated	All symptoms cleared after using lipstick containing no indelible dye 2 weeks
H. J.	12	37	4 weeks	Lips, eyelids	Lips fissured, swollen, eyelids swollen in morning	All symptoms cleared after using lipstick with no indelible dye for 1 week; when other lipsticks used, symptoms returned
R. F.	13	37	3 months	Lips	Fissured and bleeding in corners	After using lipstick containing no indelible dye for 30 days, lips normal
A. B.	14	23	6 months	Lips	Fissure, burn, peel	After using lipstick containing no indelible dye for 4 days, lips normal
J. W.	15	28	6 months	Lips	Fissure, edema, burn	After using lipstick containing no indelible dye for 3 weeks, lips normal

F. K.	16	36	Since started use of lipstick	Lips	Fissure, burning	After using lipstick containing no indelible dye for 30 days, lips normal
B. F.	17	52	3 months	Lips	Fissure, burning	After using lipstick containing no indelible dye for 6 weeks, lips normal
B. A.	18	40	1 month	Lips	Fissures	After using lipstick containing no indelible dye for 3 weeks, lips normal
E. B.	19	37	3 years	Lips	Fissures	After using lipstick containing no indelible dye for 5 days, lips normal
R. F.	20	18	Since using lipstick	Lips	Fissures	After using lipstick containing no indelible dye, lips normal
R. F.	21	25	2 months	Lips, face and body	Lips, fissured; face, acne; body, urticaria	After using lipstick containing no indelible dye and eliminating all perfumes all symptoms cleared
R. G.	22	40	10 months	Lips	Edema and pain	After using lipstick containing no indelible dye for several days, all symptoms cleared
D. L.	23	38	3 months	Lips	Edema	After using lipstick containing no indelible dye, lips immediately normal
A. O.	24	26	Several years	Lips	Fissures, edema	After using lipstick containing no indelible dye, lips normal
E. B.	25	18	Several years	Lips	Fissures, edema	After using lipstick containing no indelible dye and elimination of scented cosmetics, all symptoms cleared
M. T.	26	36	9 months	Lips, arms, neck, face	Fissures, dermatitis	After using lipstick containing no indelible dye and eliminating perfume and scented cosmetics, symptoms cleared
L. N.	27	17	6 months	Lips, chin, forehead	Lips, fissured; dermatitis on chin and forehead	All symptoms cleared after using lipstick containing no indelible dye
S. L.	28	24	Since starting to use lipstick	Lips	Dry, fissured	Symptoms cleared after using lipstick containing no indelible dye
B. M.	29	38	2 years	Lips	Corners cracked, lips fissured, edema and scaling	Improvement after use of lipstick containing no indelible dye; cleared completely in 2 weeks
P. S.	30	23	5 weeks	Lips	Edema, fissuring and scaling	After using lipstick containing no indelible dye, cleared in 1 week
E. S.	31	42	May 1944; seen Nov. 7, 1946	Lips	Edema, fissures	After use of nonindelible lipstick condition cleared in 1 week
M. B.	32	21	Dec. 1943; seen Nov. 19, 1946	Lips	Edema, fissuring and scaling; eruption about nose, eyes lacrimose and injected	After use of nonindelible dye lipstick, condition cleared in 2 weeks

Lipstick dermatitis is characterized by swelling and edema of both lips. There may also be scaling, fissuring and superficial erosions with occasional small grouped vesicles. Subjective symptoms are usually sensations of dryness, burning and tingling.

The eruption may appear after the patient has changed to a new type of lipstick, or it may suddenly appear with continued use of the same brand over a period of months or years. The precipitating factor is, of course, the idiosyncrasy to, and/or direct chemical irritation from, the indelible dyes (bromfluoresceins).

Local factors may give rise to signs and symptoms closely paralleling true cheilitis. Among the physical factors to be considered in a diagnosis of cheilitis are: trauma with contamination, salivation, light, biting or licking the lips and previous irritation of a susceptible site. The local conditions to be eliminated are: (1) herpes simplex, (2) angioneurotic edema, (3) eruptions due to drugs, (4) bullous erythema multiforme, (5) syphilitic chancres and papules, (6) leukoplakia, (7) avitaminosis, (8) eczema, (9) erysipelas, (10) malignant conditions, (11) radio-dermatitis, (12) cheilitis exfoliativa and (13) cheilitis glandularis. Generalized conditions with lip involvement to be ruled out are: (1) lupus erythematosus, (2) erythema multiforme, (3) drug eruptions, (4) pemphigus, (5) lichen planus and (6) sarcoidosis.

The 32 cases of lipstick dermatitis summarized in the table were seen in one year of private practice. The diagnosis was made on a clinical basis; confirmation of diagnosis and treatment were by elimination of bromfluorescein dyes. A lipstick was substituted which did not contain dibromfluorescein, tribromfluorescein or tetrabromfluorescein. The patients' symptoms disappeared in an average period of two weeks. The patients have remained free of symptoms to the time of writing with continued use of lipstick not containing the indelible dyes.

The factor of sensitization to light in this series of cases seems to be negligible. Only 4 of 32 patients (12.5 per cent) experienced their first symptoms in the summer. Eight (25 per cent) were vague about the seasonal onset, and the remainder (62.5 per cent) had the first attack during the winter. The patch test was not performed in this series of cases.

SUMMARY AND CONCLUSIONS

A list of reported causes of cheilitis and a review of the literature are presented. The chemistry of lipstick is discussed with special reference to possible sensitizers. Local and general factors in differential diagnosis of cheilitis are listed.

A series of 32 cases of lipstick cheilitis is presented, which were gathered from one year of practice. The diagnosis was made clinically, and treatment was by elimination of bromfluorescein dyes.

Photosensitization is considered negligible.

The use of lipstick with a nonindelible dye is a practical, safe and rapid treatment and the solution of this frequent cosmetic problem.

Lipstick dermatitis, or cheilitis due to chemical irritation, is much more common than is supposed and is often misdiagnosed or overlooked by the physician and by the patient.

Dr. Edward A. Oliver contributed valuable suggestions.

1 North Pulaski Road.

ULCERATING HEMANGIOBLASTOMA

Report of a Case

IRVING N. HOLTZMAN, M.D.
AND
DAVID M. GRAYZEL, M.D., Ph.D.
BROOKLYN

CHRONIC ulceration of the lower extremities is one of the more common perplexing problems of medical practice. The following case is reported because of the unusual histologic observations. A thorough search of recent literature failed to reveal any comparable cases.

REPORT OF A CASE

W. J., a Negro, aged 30, was first admitted on Jan. 15, 1932 for surgical treatment of a duodenal ulcer. Examination on admission revealed as an incidental discovery ulceration on the front of the left leg, occupying the entire mid-portion, 5 inches (12.7 cm.) in length and 2 inches (5 cm.) in width and covered by a firmly adherent brown crust. The surrounding skin was deeply pigmented. No discharge was noted. The patient stated that at the age of 9, following a blow to this region a sore developed which discharged pus and then pieces of bone. Frequently the lesion would heal over completely and then recur after any injury to this site. The Wassermann reaction of the blood was negative. Roentgenologic examination revealed condensation of the cortex of the tibia in this area. This was interpreted as an old, possibly syphilitic, osteomyelitis.

After a pyloroplasty for his duodenal ulcer the patient was not seen again until March 1938, when he applied for treatment of the ulceration of his leg. The lesion had discharged several pieces of bone intermittently during this interval. Roentgenologic examination showed little change in the condition as revealed in the previous examination. The Wassermann reaction was still negative. The lesion was treated conservatively as chronic osteomyelitis with little improvement until Nov. 15, 1939. Operation was then performed with excision of the ulcer and saucerization of the entire diseased area. At operation it was noted that the periosteum was thickened and that under it were several areas of necrotic bone; the remaining visible bone was decidedly eburnated. The entire area was curetted and a trough created, the periosteum was sutured and the wound closed. Infection set in and was cleared up by maggot therapy. Eventually (five months later), with the help of pinch grafts, the wound healed completely.

Gross Examination of Pathologic Specimen.—Two specimens were submitted for examination. One consisted of several flat portions of skin removed from the left leg. They had a blue-gray color and measured up to 3.5 by 3 by 0.4 cm.

From the Departments of Laboratory and Dermatology of the Jewish Hospital of Brooklyn.

Sections fixed in Bouin's solution were taken for histologic study. Accompanying these were several irregular portions of osseous tissue removed from the tibia of the left leg. These measured up to 4 by 3 by 1.5 cm. The edges were ragged and the external surfaces showed irregular depressions. Sections fixed in 10 per cent solution of formaldehyde were taken for decalcification and histologic study.

Fig. 1.—Roentgenogram of the lesion in the tibia.

Microscopic Examination of Pathologic Specimen.—In a preparation from the skin the surface appeared corrugated and was covered by stratified squamous epithelium of varying thickness with superficial keratinized layers and short blunt rete pegs. The epidermis in places was irregularly acanthotic. Scattered through the upper layer of the cutis were a few small hair follicles, and in the deeper portions, some sweat glands. The papillae were broad and there was moderate interstitial edema. Throughout the preparation were sparsely placed focal infiltra-

tions of small round cells, large mononuclear cells and occasional plasma cells, mainly perivascular. Many of the large cells were laden with golden brown granules which stained blue with Perles' reaction. The striking feature, however, was the presence, within the broadened papillae, as well as in the deeper portions of the cutis, of numerous small vascular structures, singly or in groups. The lumens were narrow and the walls relatively thick. In some areas cords of cells without lumens could be seen. The lining endothelial cells were prominent. They contained large vesicular nuclei and were often clumped around rudimentary lumens. Many of the vessels were surrounded by brown pigment, coarsely granular

Fig. 2.—Photomicrograph of the lesion in the skin. Note the many small vascular structures in the papilla and in the cutis. Hematoxylin and eosin stain; × 75.

and contained in some areas within large macrophages. This pigment stained blue with Perles' reaction. No elastic tissue could be seen with Weigert's elastic tissue stains around any of the vessels described. Preparations from the osseous tissue showed nothing of note.

Pathologic Diagnosis.—Skin from the left leg had sclerosing hemangioblastoma; osseous tissue from the left tibia was normal.

The history of injury and the clinical indolence of the lesion suggest an underlying abnormal type of granulation tissue with the abnormality inherent in

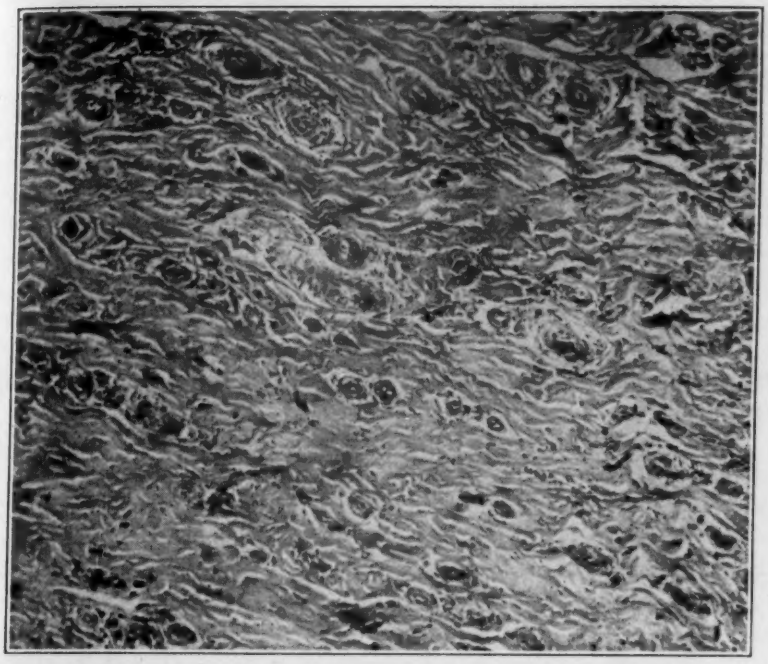

Fig. 3.—Note the vessels, many with slitlike lumens, and the pigment granules in the perivascular connective tissue. Hematoxylin and eosin stain; × 150.

Fig. 4.—Same view as in figure 3 under greater magnification. Hematoxylin and eosin stain; × 900.

the newly formed vessels. Whether this is a true neoplasm cannot be determined as yet. Pathologically the abnormality is demonstrated in the large cells forming the channels and also in the porosity of the new vessels as evidenced by the extravasated iron pigment lying outside their walls. Clinically the indolent erosive nature of the lesion suggests a neoplastic element.

SUMMARY

A chronic ulceration of the leg in an adult Negro is reported with unusual histologic observations of an abnormal type of proliferation of the blood vessels.

CUTANEOUS ERUPTIONS FROM STREPTOMYCIN

MAJOR KARL STEINER
AND
LIEUTENANT GEORGE W. FISHBURN
MEDICAL CORPS, ARMY OF THE UNITED STATES

THE TOXICITY of streptomycin has been discussed in detail by a number of authors. Cutaneous eruptions from streptomycin, however, are mentioned in only two papers. Heilman and his collaborators [1] observed "dermatitis (toxic erythema) and cutaneous eruptions of an urticarial type" and warned, "Although . . . streptomycin may be continued . . . it is exceedingly important to remember that severe dermatitis may result." These remarks were based on the observation of 40 patients. In the report on streptomycin by the National Research Council (Chester S. Keefer, chairman)[2] many more particulars on cutaneous eruptions are given. Forty-nine cutaneous eruptions were observed among 1,000 cases reported. During a period of treatment of ten days the cutaneous lesions appeared in 34 cases on any day from the second on, and especially increased incidence was not noted at any time, unless the 14 eruptions which developed on the fourth or fifth day should be interpreted as higher incidence. In 4 cases the eruptions showed up on the first, second or fifth day after the termination of treatment. In 11 cases the date of appearance of eruptions was not specified. In only 18 of the 49 cutaneous reactions were the durations noted: 8 lasted one day, 1 each seven and nine days, respectively, and 8 for periods of two to five days (3 for two days, 2 for three days, 1 for four days and 2 for five days). Erythematous, urticarial, maculopapular and hemorrhagic reactions, with and without fever, were seen, but there were no rashes of a specific character. Four patients who received a single injection of streptomycin a few weeks after the first series presented recurrences of cutaneous eruptions. In 1 case an injection of 0.0375 Gm. which was given

From the Dermatological Section and the Tuberculosis Section of Fitzsimmons General Hospital, Denver.

1. Heilman, D. H.; Heilman, F. R.; Hinshaw, H. C.; Nichols, D. R., and Herrell, W. E.: Streptomycin: Absorption, Diffusion, Excretion and Toxicity, Am. J. M. Sc. **210**:576-584 (Nov.) 1945.

2. Keefer, C. S.: Streptomycin in the Treatment of Infections: A Report of One Thousand Cases, J. A. M. A. **132**:70-76 (Sept. 14) 1946.

twenty days after the last injection resulted in slight fever. On the next day the same amount of streptomycin was injected and was followed by a cutaneous eruption over the areas of previous involvement and by an increase of eosinophils from 2 per cent to 10 per cent. The rash disappeared promptly, but the eosinophilia persisted. In another case an injection of 0.375 Gm. of streptomycin on the thirty-second day after termination of the previous treatment was followed within thirty-six hours by the reappearance of the rash. Three days later a single injection did not produce a rash, and the streptomycin was continued, but in this case the eosinophilia persisted. The report notes that the longer the interval of time between the different treatments the less likely is a second reaction. "In most instances it is well to stop the streptomycin if a skin eruption appears; certainly the dose should be reduced, and if treatment is continued it should be done with care and caution."

Mention should be made of "immediate toxic effects" in the form of "transient urticaria" of a mild or moderate character as seen by Zintel and his collaborators.[3] For the avoidance of this urticaria slow administration was recommended by the authors. This type of reaction seems nonspecific and cannot strictly be ascribed to streptomycin, for which reason it will not be discussed further.

A few observations on cutaneous rashes following administration of streptomycin, which we made in the summer of 1946, allowed us to come to certain conclusions that are at some variance with the opinions expressed in the report of the National Research Council[2] and by Heilman and his collaborators.[1] We think that the publication of our observations might be of practical interest in the management of treatment with streptomycin.

ERUPTIONS FROM STREPTOMYCIN

Among 33 patients with pulmonary tuberculosis who were treated with streptomycin, 31 were receiving 0.3 Gm. and 2 were receiving 0.5 Gm. intramuscularly every four hours. In addition, 3 of these patients were receiving 0.5 Gm. daily by nebulization. Thirty-one of the total number were male and 2 were female. Six instances of cutaneous eruption were noted. Four of the patients with eruption were receiving 0.3 Gm. every four hours, 1 was receiving 0.5 Gm. every four hours, and 1 was receiving 0.3 Gm. every four hours plus 0.5 Gm. daily by nebulization. One of the 6 patients with rash was Mexican; the others were white. All cases of rash occurred in male patients. The table shows all other particulars.

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3. Zintel, H. A.; Flippin, H. F.; Nichols, A. C.; Wiley, M. M., and Rhoads, J. E.: Studies on Streptomycin in Man: I. Absorption, Distribution, Excretion, and Toxicity, Am. J. M. Sc. **210**:421-430 (Oct.) 1945.

Summary of Data Concerning Six Cases of Cutaneous Eruption from Treatment with Streptomycin for Pulmonary Tuberculosis

Patient	Age	Diagnosis	Allergic History	Day of Onset of Rash	Character of Rash	Temperature	Eosinophils, %	Duration of Rash, Days	Interval of Interruption of Treatment; Dosage Resumed	Duration of Further Treatment
A. Q.	21	Infiltration and cavitation of upper lobe, right lung; bronchogenic spread to upper lobe, left lung	Hay fever; mother: urticaria	7th	Generalized macular roseola, morbilliform, nonpruritic	100 F.	11	2	2 days; ½ dose	4 mo. (completed)
C. R. A.	25	Cavitation of upper lobe, right lung; bronchogenic spread to lower lobe, left lung	None	8th	Maculopapular, particularly on upper part of trunk and on arms; nonpruritic	Normal	13	6	No interruption	4 mo. (completed)
R. R.	25	Nodular in upper lobe, right lung; minimal in apex, left lung; cavity in 1st interspace, right lung; lesion in larynx	Sister: hay fever	9th	Generalized maculopapular, follicular; pruritic	Normal	12	6	36 hr.; same dose	4 mo. (completed)
D. J. S.	22	Right lung, intraclavicular with cavity	Migraine (?)	8th	Generalized macular and rubeoliform, mainly on trunk	101-102 F.	21	4	No interruption	4 mo. (completed)
H. R. H.	49	Bilateral fibrous (?); tuberculosis of urinary bladder	Hay fever	7th	Generalized, including palms and soles, erythema-multiforme-like, severe pruritus	103 F.	2	3	1 day; 1/10 dose	4 mo. (completed)
E. R. O.	25	Right lung, nodular with cavities in upper lobe; bronchogenic spread to upper lobe, left lung	None	26th	Erythema-multiforme-like on arms and legs; angioneurotic edema of eyelids and lips	Normal	22	7	1 wk.; 1/10 dose	4 mo. (completed)

From the table can be seen that 3 or probably 4 of the patients had a personal or family history of allergy. In 5 patients the rash appeared on the seventh, eighth or ninth day after the commencement of the treatment. In character the eruptions were, as described by the previous observers, roseola-like, maculopapular, morbilliform, scarlatiniform, erythema-multiforme-like, urticarial, sometimes follicular, usually generalized but always more pronounced on the upper part of the trunk and on the arms; they were sometimes moderately pruritic but not so pruritic as the urticaria from penicillin. Hemorrhagic eruptions were not noted. The duration varied from two to seven days. The eruptions were apparently little influenced by treatment, which in the main was with calcium gluconate administered intravenously, "benadryl hydrochloride" N. N. R. (diphenhydramine hydrochloride) and ephedrine.

An increase in the number of eosinophils, up to 22 per cent, was present in all cases. Three patients did not show elevation of temperature. A moderate rise up to 101 to 102 F. could be observed in 2 patients. One patient had a temperature of 103 F. However, in these last 3 patients there was a return to the usual subfebrile temperatures within one day to two days. Mild to moderate toxic reactions, including nausea and tinnitus, occurred in almost all patients who were treated with streptomycin.

In 2 of the 6 cases the treatment with streptomycin was continued in spite of the rash. In the other cases it was resumed after one day, thirty-six hours, two days and one week, respectively. In 1 of these cases a single dose of 0.15 Gm. was given for the first two days. In another case one tenth of the usual dose was administered in the beginning, to be increased daily up to the normal dosage. In a third case, in which the patient had received 3 Gm. daily instead of the 1.8 Gm. which was otherwise injected, 0.05 Gm. was given on the first day, and the amount was increased by 0.1 Gm. per dose every day until the old level had been reached. In the fourth case treatment was resumed at the previous level. All 6 patients finished a full four months' course of treatment with streptomycin. In no case was there a recurrence of the cutaneous eruption, and no particular toxic or allergic reaction developed subsequently.

One more patient had cutaneous eruptions after treatment with streptomycin. This patient differed in a few aspects from the 6 discussed so far.

REPORT OF A CASE

A 34 year old white woman of a somewhat psychoneurotic personality had a history of eight years of hay fever. She was admitted to the hospital with a diagnosis of minimal, inactive, reinfection type of pulmonary tuberculosis of the upper lobe of the left lung. In addition, she had chronic pyelitis of the right kidney with acute exacerbations. Bacterium coli, Streptococcus viridans and

hemolytic staphylococci were observed in the urine discharged by catheterization. Because of this infection she received sulfadiazine and later penicillin, after which she had severe urticaria. Since the urinary infection did not clear up, the patient received 1 Gm. of streptomycin a day beginning May 9, 1946, after the urticaria had cleared up. On May 16, seven days after the start of treatment with streptomycin, there appeared a slightly raised erythema on the right forearm, at the site of a Mantoux test done on Jan. 31, 1946 that had elicited a positive reaction of 1 plus. On May 17 the erythema became more pronounced and raised and rather circumscribed. From this erythema an irregular, macular and patchy, bright pink rash was spreading up the entire arm, especially on the flexor surface. On the left arm there was an erythema of the same character but less pronounced. In the course of the day there was further spread of the eruption, until a generalized, severely pruritic urticaria had developed. Streptomycin was discontinued, and the patient received epinephrine. On the next day there was some improvement, and the urticaria subsided gradually until the end of the month. No particular systemic reactions accompanied the cutaneous eruption.

More than a month later, in July, the patient received another course of streptomycin for ten days, and she again experienced a rash, this time after three days, that lasted eight to ten days. Again there were no other systemic reactions. A repetition of the treatment with penicillin did not cause another cutaneous eruption.

COMMENT

As compared with the observations of the National Research Council [2] this report necessarily suffers from the error of the small number of cases which were studied. Furthermore, confirmation on the basis of much more material is required to verify the following conclusions. This paper is, therefore, in the nature of a preliminary report to stimulate further investigations.

It seems that the number of cutaneous eruptions from streptomycin can be much greater than was reported by the National Research Council. Six rashes in 33 cases (18.2 per cent) occurred in our series as compared with only 49 in 1,000 cases of the Council (4.9 per cent). It cannot be said whether this was due to a different selection of the cases or to the employment of another brand of streptomycin, but the difference appears to be too great to be accidental only.

In 6 of the 7 reported cases the eruptions appeared on the seventh, eighth or ninth day after the initiation of treatment. This is in striking contrast with the observations of the National Research Council. When considering this fact we could not fail to think of the "erythema of the ninth day" as described by Milian and explained by him on the basis of "biotropism." Whether this interpretation applies to the eruptions from streptomycin is as yet impossible to say. The eosinophilia, which was frequently considerable, certainly points to an allergic mechanism in the development of the rashes, as does the "accelerated reaction time" on readministration of streptomycin, which was observed by the investigators of the Council as well as by us. It seems safe to say that the eruptions from streptomycin are not of a toxic but of an allergic nature.

Because of their resemblance to erythema of the ninth day, as shown by the time of their eruption, by their transitoriness and by their uncharacteristic appearance, the rashes were not taken as contraindications against the continuation of the treatment. The absence of systemic reactions in all but 1 case tended to strengthen this attitude, which was further justified by the results of additional treatments that were given either without any interruption or after a discontinuation of one or two days. The full dosage could then be given, after a short transitional period, for a long time without untoward reactions. This result seems most important to us. It means that cutaneous reactions after administration of streptomycin, at least those apparently frequent eruptions of the character of erythema of the ninth day, need not deter one from the continuation of the treatment and, at the worst, should only be indications for short interruption and resumption of treatment with usually smaller gradually increasing doses.

A satisfactory explanation of the flare-up of the reaction to the Mantoux test in the 34 year old woman cannot be offered. Allergy seems out of the question, since the active agent was nonspecific. A process of the type of the Sanarelli-Shwartzman phenomenon might perhaps account for this reaction.

SUMMARY

Seven cases of cutaneous eruptions after treatment with streptomycin are discussed. These eruptions were, in general, of the character of the erythema of the ninth day. The allergic nature of the eruptions seemed unquestionable. Because of the mildness of the eruptions and on account of the essential absence of systemic reactions, treatment with streptomycin was continued and there were not any untoward sequelae. It is therefore suggested that eruptions of the described type should not be considered as contraindications against further necessary or desirable treatment with streptomycin.

35 Fort Washington Avenue, New York 32.

General Hospital, Denver 8.

DEVELOPMENT OF SQUAMOUS CELL EPITHELIOMA IN EPIDERMOLYSIS BULLOSA

Report of a Case

LAWRENCE K. HALPERN, M.D.
ST. LOUIS

EPITHELIOMA has been known to occur in the lesions of such chronic cutaneous diseases as psoriasis, eczema, hypertrophic lichen planus and blastomycosis. The resulting tumor may be either basal or squamous cell epithelioma.

It is also well known that epithelioma may develop in scar tissue resulting from such causes as burns of varied origin, trauma, syphilis, tuberculosis, lupus vulgaris and lupus erythematosus. When scar tissue undergoes carcinomatous change it is generally of the squamous cell type. Obviously then, there is nothing startling in reporting the development of carcinomatous change in a lesion of chronic dermatosis or in cicatricial tissue. However, the case to be reported would appear to be of interest for two reasons. First, a search of the literature did not disclose a report of the occurrence of epithelioma as a sequel of epidermolysis bullosa, and, second, the development of bilateral squamous cell epithelioma of the lower extremities is rather unusual.

REPORT OF A CASE

History.—O. M., a 53 year old white man, was first seen in the Skin Clinic of the Barnard Free Skin and Cancer Hospital on April 17, 1946. The patient stated that about one year previously he was struck on the right leg by a stick when he slipped off a scaffolding. The stick penetrated the skin, and a "sore" developed. This failed to heal, gradually enlarged and became somewhat painful. The ulcerated area drained a small amount of foul-smelling pus. A few months after injuring the right leg, he experienced a minor trauma to the left leg, above the heel. Apparently this was a rather insignificant injury, because the patient was unable to recall the specific details. He noticed a small "wartlike" growth, which gradually enlarged. This lesion did not ulcerate.

The patient stated that since infancy he had had blisters on the legs, dorsum of the hands and extensor surface of the elbows after slight trauma. The blisters would dry up in several days, leaving a dark red scarred area. As long as he could recall, the skin of the legs had been scarred, pigmented and scaly. The

Studies, observations and reports from the Dermatologic Department of the Barnard Free Skin and Cancer Hospital and the Washington University School of Medicine (service of Dr. M. F. Engman Sr.).

hands were not as seriously involved as the legs. Blisters did not develop after trauma elsewhere on the body.

On being questioned regarding family history, he stated that he had a brother, aged 50 years, and a sister, aged 47 years, in both of whom blisters tended to develop on the legs, elbows and hands after slight trauma. According to the patient, their hands and legs became scarred, pigmented and scaly, but neither one experienced the ulcerating and fungating growths to be described herein. There was one other sibling, a sister, whose skin was entirely normal. His parents and all other known relatives were thought to be free from the lesions of epidermolysis bullosa. However, the accuracy of this observation is open to question.

Physical Examination.—The patient was in good general health. He was fairly well developed and well nourished. His height was 70 inches (177.8 cm.) and

Fig. 1.—*A*, anterior view of the legs, showing scaling, scarring and squamous cell epithelioma of the right leg. *B*, lateral view of the right leg, showing large squamous cell epithelioma. *C*, posterior view of the left leg, showing squamous cell epithelioma above the heel.

weight 152 pounds (69 Kg.). Most of his teeth were missing, and the remaining teeth were infected. The liver was palpable about 5 cm. below the right costal margin. It was smooth and not tender. The remainder of the general physical examination revealed no abnormalities except as mentioned later in this report.

Dermatologic Examination.—Mouth: There was a superficial plaque of leukoplakia, 1 cm. long, on the left corner of the lower lip.

Upper Extremities: The lesions were limited to the elbows and hands. The skin over the extensor surface of the elbows was dark red, atrophic, wrinkled and scarred. It had the appearance of cigaret paper. The skin of the dorsa of

both hands was atrophic, scarred and red. The palms were normal except for scars from electric burns experienced thirty-five years previously.

Lower Extremities: The lesions were limited to the legs, from the knees to the feet. The thighs were entirely clear. The skin of both legs was deep red, scarred, atrophic and scaly (fig. 1 *A*). A few blisters were noted. The skin over the patellas was thin, atrophic and wrinkled. On the right leg, in the middle

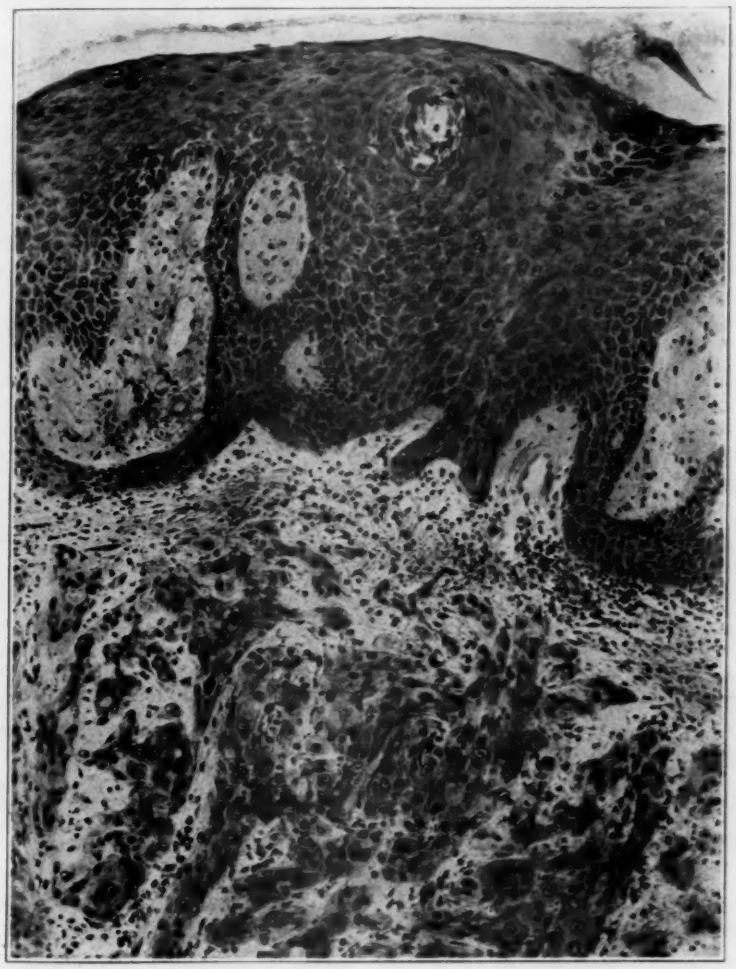

Fig. 2.—Photomicrograph of a section from the lesion on the right leg, showing squamous cell epithelioma.

third on the lateral aspect, there was a large irregularly shaped ulcer (fig. 1 *B*). It measured approximately 20 cm. in its transverse axis and 10 cm. in its vertical axis. The edge of the lesion was hard, indurated and elevated. The center of the lesion had a moist verrucous appearance, and there was a moderate amount of foul-smelling pus and necrosis. On the left leg, about 2.5 cm. above the level of the malleoli on the posterior surface, there was a dry verrucous, hypertrophic

lesion, about 5 cm. in diameter and elevated about 1.5 cm. (fig. 1 *C*). It had not ulcerated. There was a hard discrete nontender lymph node, the size of an almond, in the left inguinal region and a slightly smaller one on the right side.

Laboratory Examination.—Urinalysis revealed no abnormality except for a slight trace of albumin. The Kahn reaction was reported negative. Examination of the blood showed the hemoglobin to be 14.5 Gm. per hundred cubic centimeters,

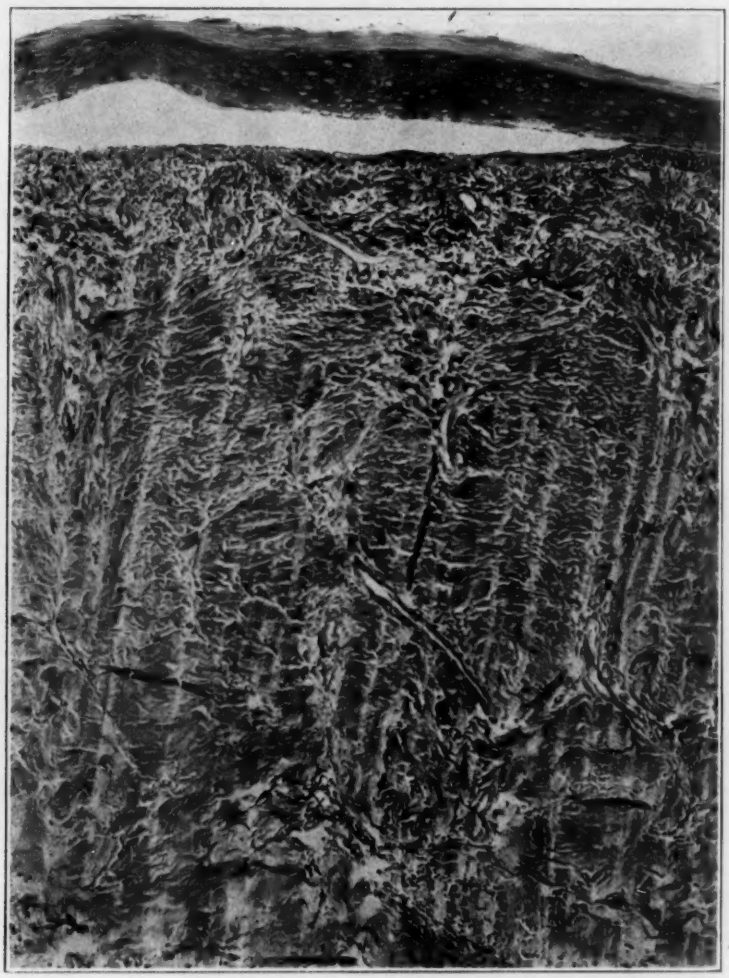

Fig. 3.—Photomicrograph of a section from the skin of the left leg, which was not involved by cancer. The section is stained with Weigert's elastic tissue stain and shows changes consistent with epidermolysis bullosa. The vesicle at the dermal-epidermal junction, the absence of elastic tissue in the upper portion of the dermis and the fragmentation of elastic tissue in the lower portion of the dermis may also be noted.

the red blood cell count 5,530,000, the white blood cell count 8,650 and the differential white blood cell count normal.

Roentgenologic examination of the lungs revealed them to be essentially normal, with no evidence of metastasis. Roentgenograms of the legs showed thickening and roughening of the periosteum of both tibias, but no definite evidence of metastasis.

Histologic Examination.—A specimen taken from the edge of the ulcer of the right leg (fig. 2) showed the epidermis to be intact, and throughout most of the section it was acanthotic. In the dermis, however, extending from just beneath the epidermis throughout the entire thickness of the corium, were islands and strands of squamous cell epithelioma. The cells making up these tumor masses were moderately well differentiated, and there were numerous epithelial pearls. Mitotic figures were numerous, and a moderate accompanying chronic inflammatory infiltrate was present. The skin that was not involved by cancer at one end of the section showed changes consistent with epidermolysis bullosa.

A specimen from the left leg through the scarred area and apparently normal skin (fig. 3) showed moderate hypertrophy in the stratum corneum, but the other layers of the epidermis were essentially unchanged. However, the rete pegs were short and stubby and in places completely obliterated. In one area a long narrow vesicle, which extended through two low power fields of the microscope, was present. It was filled with fibrin, red cells and and a few leukocytes. The dermis showed moderate edema, and the blood vessels and lymph spaces were dilated. A moderate perivascular cellular infiltrate was present, which was made up of lymphocytes, plasma cells and mononuclear cells. The infiltrate was somewhat more dense immediately under the vesicle. The collagen bundles were slightly thickened, but this change was not as pronounced as that usually seen in scar tissue.

A Weigert stain for elastic tissue showed an absence of this tissue in the upper third of the dermis throughout the section. Immediately under the vesicle the absence of elastic tissue was more extensive. In the lower part of the dermis the fibers were fragmented.

In the specimen from the verrucous lesion of the left leg the section showed intense hyperkeratosis at the surface. The epidermis as a whole was extremely hyperplastic and distorted. Extending into the dermis were irregular masses of squamous cells, which were well differentiated. Only a few mitotic figures were observed. Some of the masses contained epithelial pearls. There was relatively little dermis included in the section, but a chronic inflammatory cellular infiltrate was present about the masses of squamous cells. Although the specimen was superficial, it was indicative of squamous cell epithelioma.

Course and Treatment.—The patient was seen in consultation by the surgical staff. Careful consideration was given to the possibility that the patient might have difficulty wearing an artificial limb because of his basic disease, epidermolysis bullosa. However, because of the size of the lesion it was recommended that the right leg be amputated and that an attempt be made to save the left leg by excision of the tumor followed by plastic repair. The patient did not consent to operation and was discharged from the hospital at his own request.

COMMENT

The patient presented a typical clinical picture of epidermolysis bullosa, which was confirmed by histologic observations. He sustained minor trauma to his legs and hands almost every day of his life. This usually resulted in the development of bullae, which promptly healed and were followed by scarring, pigmentation and atrophy. It may be

assumed that the severer trauma to the right leg caused an ulcer in the scarred skin, which progressed so that at the time of examination there was a well advanced and extensive squamous cell epithelioma. The verrucous lesion of the left leg, which followed only slight trauma, did not ulcerate, but showed microscopic changes consistent with early squamous cell epithelioma.

SUMMARY

A search of the available literature did not disclose a report of the development of cancer in lesions of epidermolysis bullosa.

A case of epidermolysis bullosa in which bilateral squamous cell epithelioma of the legs developed is presented.

DISSEMINATED ULCERATING SPOROTRICHOSIS WITH WIDESPREAD VISCERAL INVOLVEMENT

Report of a Case

WILLIAM T. COLLINS, M.D.
CINCINNATI

A REVIEW of the American literature on sporotrichosis has revealed few cases with visceral involvement. The present report is of a case in which there were widespread visceral lesions.

The number of cases of sporotrichosis reported in this country now total over 200, the majority being from the Mississippi Valley region. The organism is widely distributed as a saprophyte on vegetation, and Foerster [1] has emphasized the occupational hazard of sporotrichosis among farmers and horticulturists and the importance of the barberry shrub as a source of infection.

Sporotrichosis is a disease with several clinical types, which are usually classified as follows:

1. Localized type: This is the commonest form in the United States. A primary ulcerated lesion, or chancre, appears usually on the hands or forearms and is followed after several days by the development of circumscribed hard painless subcutaneous nodules, which frequently ulcerate, along the course of the regional lymphatic vessels.

2. Disseminated gummatous type: This variety is more frequently encountered in France and is manifested by widely scattered hard painless subcutaneous nodules that soften and form abscesses, but rarely ulcerate unless traumatized.

3. Disseminated ulcerative type: This form is similar to the preceding type but is characterized by early spontaneous ulceration, producing lesions which resemble the ulcerative lesions of tuberculosis and tertiary syphilis.

4. Extracutaneous type: The mucous membranes, the muscles, the bones and joints, the eyes and rarely the viscera may be invaded by the organism.

From the Departments of Dermatology, Bacteriology and Pathology, Cincinnati General Hospital.

1. Foerster, H. R.: Sporotrichosis: Occupational Dermatosis, J. A. M. A. **87**:1605-1608 (Nov. 13) 1926.

Microscopically, the lesion of sporotrichosis is described by various authors [2] as a granuloma, consisting of a central zone of necrosis and granulation, a middle zone of epithelioid and multinucleated giant cells and a peripheral zone of lymphocytes. Polymorphonuclear leukocytic reaction is not characteristic, unless ulceration of the skin or necrosis of the lesion has occurred. Healing takes place by proliferation of connective tissue and scarring. Most authors emphasize the difficulty of detecting the organisms in tissue sections.

In 1898, Schenck [3] described the first case of sporotrichosis in the literature and Smith tentatively classified the organism isolated as a member of the genus Sporotrichum. Two years later, Hektoen and Perkins [4] reported another authentic case and designated the name Sporotrichum schencki for the organism. In practically all the recorded cases in the United States, this organism has been considered the specific causative agent.

In 1921, Warfield [5] reported a case of disseminated gummatous sporotrichosis in a young Negro man, in which "there was a nodule in the right lung suspected on physical examination, seen in the roentgen-ray plate and confirmed at autopsy culturally and histologically." This is the first report of such a case in this country.

Hyslop and his co-workers,[6] in 1926, reported a fatal case of chronic meningitis in a 15 year old white girl. The diagnosis of meningitis associated with sporotrichosis was based on the presence of spores and mycelial forms in the spinal fluid, although cultures and inoculations in animals were negative. Autopsy revealed a chronic diffuse leptomeningitis, and microscopically foci of mycelia with spore inclusions were observed in the meninges.

In 1927, Forbus [7] described a fatal case of pulmonary sporotrichosis in a middle-aged white woman who had had pulmonary symptoms for several years. At autopsy, cultures were taken from lesions in the lungs and Sporotrichum was isolated. Spore and filamentous forms of the organism were observed in smears from the lesions. The spleen was observed to contain tubercle-like nodules similar to the nodules in the lungs, but cultures were not taken and the causative agent could not be identified microscopically.

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2. Forbus, W. D.: Reaction to Injury, Baltimore, Williams & Wilkins Company, 1943, p. 749. Ash, J. E., and Spitz, S.: Pathology of Tropical Diseases, Philadelphia, W. B. Saunders Company, 1945, p. 155.

3. Schenck, B. R.: Bull. Johns Hopkins Hosp. **9**:286, 1898.

4. Hektoen, L., and Perkins, C. F.: J. Exper. Med. **5**:77, 1900.

5. Warfield, L. M.: Am. J. M. Sc. **164**:72, 1922.

6. Hyslop, G. H.; Neal, J. B.; Kraus, W. M., and Hillman, O.: Am. J. M. Sc. **172**:726, 1926.

7. Forbus, W. D.: Am. Rev. Tuberc. **16**:599, 1927.

Two more cases of pulmonary sporotrichosis were reported by Singer [8] in 1928. In one, the diagnosis was based on the presence of miliary nodules in roentgenogram of the chest, pleural effusion, negative reactions in sputum tests for tubercle bacilli, Sporotrichum in pus aspirated from subcutaneous abscesses and improvement in the cutaneous and pulmonary lesions following potassium iodide therapy. In the other case, the evidence consisted of a proved cutaneous infection by Sporotrichum, an empyema of the pleural cavity, which communicated with a subcutaneous abscess, and improvement following the use of potassium iodide. Considerable doubt is cast on the diagnosis in the second case by the discovery of tubercle bacilli in the empyema fluid, but Singer expressed the opinion that both diseases were present in the lung.

In 1935, Moore and Kile [9] reported a case of generalized cutaneous sporotrichosis with roentgenologic evidence of extensive infiltration of both lungs, which decreased greatly after medication with potassium iodide.

REPORT OF A CASE

History.—A 67 year old white man was admitted to the Cincinnati General Hospital on Sept. 26, 1945. The patient's past history and family history were irrelevant. He had been the manager of a local theater for seventeen years, but had been retired for the past few years.

Two months before admission the patient experienced pain and swelling in the left knee, which gradually disappeared after medication with "pills and liquid medicine" for a period of one to two weeks. Three weeks before admission numerous small red papules appeared on his arms and then slowly increased in number to cover the entire body, including the face. The papules rapidly enlarged, and many developed into ulcers. The patient was entirely asymptomatic, aside from the presence of the lesions.

Physical Examination.—The patient was well nourished and did not appear acutely ill. Numerous lesions, varying from small erythematous papules to large blood-crusted ulcers, were present on the trunk, face and extremities. The superficial lymph nodes were not enlarged. Resonance and breathing sounds were normal over both pulmonary fields. The edges of the liver and spleen were palpable 3 and 4 fingerbreadths, respectively, below the costal margins, but were smooth and not tender.

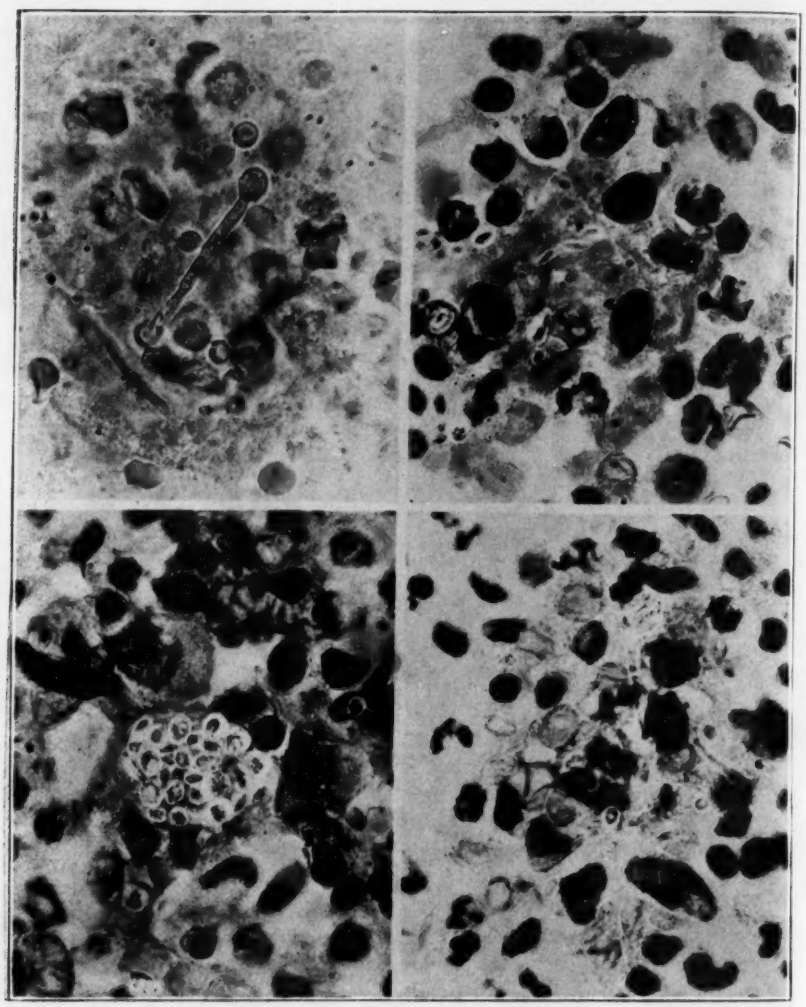
Laboratory Data.—The blood and urine were normal, as shown in analyses, throughout the course of hospitalization. Reaction to Wassermann and tuberculin tests (purified protein derivative numbers 1 and 2) were negative. Examination of the sputum revealed no acid-fast bacilli. The level of serum protein was 5.74 Gm. per hundred cubic centimeters. The spinal fluid contained 37 mg. of protein per hundred cubic centimeters and 20 white blood cells per cubic millimeter, but no organisms were observed and the fluid was not cultured. Staphylococcus aureus was isolated from cultures of the cutaneous lesions. A roentgenogram of the chest

8. Singer, J. J.: Am. Rev. Tuberc. **18**:438, 1928.

9. Moore, M., and Kile, R. L.: Generalized, Subcutaneous Gummatous Ulcerating Sporotrichosis, Arch. Dermat. & Syph. **31**:672-685 (May) 1935.

revealed increased hilar markings with an old calcification in the apex of the lower lobe of the right lung. Biopsy of cutaneous lesion showed a tuberculoid type of reaction with foreign body giant cells, epithelioid cells, plasma cells, lymphocytes and polymorphonuclear leukocytes.

Hospital Course.—The temperature remained within normal range throughout the entire stay in the hospital. The patient's general condition remained good up to



Photomicrographs of Sporotrichum schencki in splenic pulp, reduced from initial magnifications of 1350 diameters. Upper left, Sporotrichum schencki in splenic pulp in unstained sealed preparation, showing the germination of conidia, formation of a septate hypha and production of lateral and terminal conidia from it. The septum is visible just below the point of origin of the lateral conidium. Upper right, spherical, pyriform and cigar-shaped conidia in splenic pulp. Impression smear stained with hematoxylin and eosin. Lower left, cluster of yeastlike cells in impression smear of splenic pulp, showing a hyaline matrix. Lower right, portions of branched septate mycelia are visible, as well as spherical and pyriform conidia, in impression smear.

about five days before death, at which time he refused food, became weak and progressed rapidly downhill to death, on Oct. 24, 1945.

Necropsy.—Necropsy was performed twenty hours after death. The skin over the entire body and face exhibited numerous circular sharply demarcated ulcerations measuring 0.5 to 2 cm. in diameter. Scattered between the ulcerations were erythematous papules 2 to 3 mm. in diameter. The peritoneal cavity was lined by a smooth glistening membrane and contained 1,500 cc. of clear, yellowish brown fluid. The heart displayed moderate dilatation of the right atrium and ventricle and calcareous sclerosis of the cusps of the aortic valve. The lungs weighed 790 and 575 Gm., right and left respectively. The lower lobe of the right lung and the upper lobes of both lungs contained confluent areas of pneumonic consolidation. The symmetrically enlarged spleen, weighing 1,125 Gm., was covered by a smooth translucent tense capsule, and sections revealed a mushy, reddish tan pulp, in which the normal markings were obliterated. Attached to the tail of the pancreas was an accessory spleen, which measured 1.5 by 2 cm. The liver weighed 2,025 Gm., and its cut surface was firm, slightly congested and reddish tan. No abnormalities were observed grossly in the remaining viscera or brain.

Microscopic Examination.—The cutaneous lesions, which were located in the papillary corium, the reticular corium adjacent to the sebaceous and sweat glands and the subcutaneous tissue, consisted of focal areas of necrosis and a predominant cellular reaction of macrophages, which were distended with organisms. Lymphocytes were scattered between the lesions, but polymorphonuclear leukocytic reaction, formation of multinucleated giant cells and fibroblastic proliferation were absent. Many of the superficial lesions elevated and flattened the overlying epidermis, and several were ulcerated and covered with a purulent exudate.

The lymphoid follicles of the spleen were poorly defined and contained focal areas of necrosis, infiltrated with macrophages and surrounded by proliferating connective tissue in which hemosiderin was deposited. A mild reaction of polymorphonuclear leukocytes, lymphocytes and an occasional multinucleated giant cell was observed in a few of the lesions. These lesions principally involved the lymphoid follicles, but frequently extended into the adjacent pulp. Numerous organisms were disseminated throughout the spleen and were in the focal lesions both intracellularly and extracellularly and in the reticuloendothelial cells of the pulp.

Scattered throughout the liver were many submiliary foci of necrosis, which were located chiefly in the peripheral half of the lobules and were infiltrated with macrophages, lymphocytes, polymorphonuclear leukocytes and occasionally multinucleated giant cells. Organisms were present both within the macrophages and free in the tissue spaces. Other lesions, which were located chiefly around the portal triads, exhibited a minimal cellular reaction and a varying degree of fibrosis and hemosiderosis, producing a picture similar to that of early portal cirrhosis.

Miliary lesions similar to the lesions in the liver were also seen in the myocardium, the renal cortices and medullas, the suprarenal cortices and the cerebral cortex. The bone marrow, which was hyperplastic, was massively invaded by the organisms.

The other pertinent microscopic observations were acute bronchitis and lobular pneumonia, with evidence of terminal aspiration and moderate diffuse perivascular fibrosis of the myocardium.

A fresh specimen of splenic pulp was examined and cultured by Dr. Lee Foshay, Director of the Bacteriology Service, who contributed the following information.

Examination of splenic pulp fluid under a sealed cover slip revealed numerous spherical and ovoid conidia and rare elongated ellipsoidal ones. Many spores had germinated. The presence of branched septate hyphae offered indisputable proof that growth had far exceeded the germ tube stage. Furthermore, the frequent formation of lateral and terminal conidia by a moderate number of the longer hyphae and by a few of the shorter ones offered convincing evidence of completion of the life cycle phase that is familiar on culture mediums. An example of formation of conidia by a short septate unbranched hypha is illustrated.

Impression smears of splenic pulp, stained with hematoxylin and eosin, revealed all the aforementioned features and, in addition, rare examples of the forms usually described as cigar shaped in both intracellular and extracellular locations. A striking feature of the stained smears was a clumping together of spherical, pyriform and ellipsoidal cells within what seemed to be a clear hyaline matrix. The appearance of the clumps was reminiscent of that often seen in torulosis.

Cultures of the splenic pulp on Sabouraud's glucose agar were incubated at 37 C. and at room temperature. The former showed no growth, nor was there growth later after pure cultures were incubated at 37 C. on either Sabouraud's medium or on meat infusion agar. The cultures on Sabouraud's medium that were incubated at room temperature revealed growth after forty-eight hours. At first small and white and without aerial hyphae, the colonies grew rapidly, developed deep brown to blackish brown pigment by the fourth day and showed the characteristic convolute, or cerebriform, appearance after the fifth day. Repeated transfers of pure pigmented colonies to meat infusion agar, incubated at room temperature, always produced unpigmented colonies. Microscopic examinations of cultures showed the delicate, irregularly branched, septate hyphae with intercalated and terminal clusters of ovoid or pyriform conidia that are characteristic of S. schencki.

Subsequently, subcultures of the organism were examined by Conant, Moore and Emmons. All confirmed the diagnosis of S. schenki.

SUMMARY

A case of disseminated cutaneous and visceral infection with Sporotrichum schenki is reported in a 67 year old white man. The fatal infection began about two months prior to death with a swelling of the knee, followed five weeks later by a generalized cutaneous eruption of papular and later ulcerative lesions.

BLASTOMYCOSIS, NORTH AMERICAN TYPE

A Proved Case from the European Continent

MELVIN BRODY, M.D.
CLEVELAND

NORTH AMERICAN blastomycosis is a disease almost exclusively limited to the United States. Martin and Smith,[1] in their exhaustive review of the literature, read of only 2 proved cases reported outside the United States, 1 in Canada and 1 in England. The foreign literature contains many reports of blastomycosis of the Gilchrist or North American type, but the diseases are described and diagnosed so inadequately that they cannot be definitely accepted as the Gilchrist type.[2] For example, in no foreign cases are differential cultures described. It is therefore of interest to report the first proved case of North American blastomycosis from the European Continent.

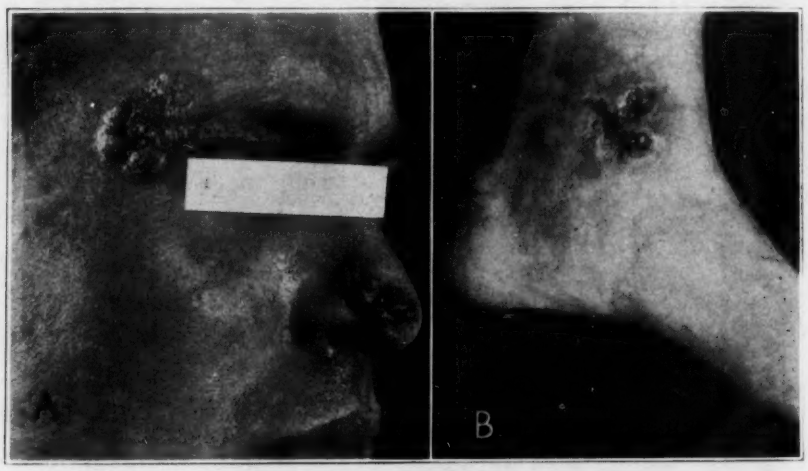
REPORT OF A CASE

A 24 year old man was inducted into the Army in December 1942. He felt well at that time. In December 1943 he was sent to England, where he remained for nine months. He was then sent to France, and he performed full duty from September 1944 to July 1945, when he first became ill. He experienced symptoms of atypical pneumonia, associated with fever, night sweats, hemoptysis and pain in the right side of the chest. A roentgenogram of the chest revealed a large area of consolidation in the medial portion of the upper lobe of the right lung. The results of repeated examinations of sputum for acid-fast bacilli were negative. The patient was evacuated to the United States and arrived at Kennedy General Hospital on August 22. At that time, in addition to his pulmonary disease, the patient presented cutaneous lesions on the right side of the nose and on the right eyebrow, which had appeared six weeks previously while he was in France. He also had a red tender subcutaneous swelling in the region of the medial malleolus of the left leg of three weeks' duration. The facial lesions were crusted, elevated and papulopustular, with heaped-up margins. The subcutaneous lesion on the left ankle was incised, and bloody necrotic material was evacuated. Cultures from the abscess and from the facial lesions showed typical Blastomyces dermatitidis. On histologic examination the lesion on the nose was described as " . . . hypertrophy of the epidermis with a diffuse inflammatory reaction in the cutis. There were

1. Martin, D. S., and Smith, D. T.: Blastomycosis (American Blastomycosis, Gilchrist's Disease): I. Review of the Literature, Am. Rev. Tuberc. **39**:275-304 (March) 1939.

2. Conant, N. F., and others: Manual of Clinical Mycology, National Research Council, Division of Medical Sciences, Philadelphia, W. B. Saunders Company, 1944, p. 25.

numerous microabscesses throughout the tissue, with foreign body giant cells, and round budding organisms with double refractile walls. The diagnosis was blastomycosis." During his stay at Kennedy General Hospital numerous examinations of sputum were made, but they revealed nothing of significance. The patient was treated with penicillin and sulfadiazine, and his pulmonary disease gradually cleared completely after three months of treatment. The cutaneous lesions were unimproved. A roentgenogram of the left leg showed a localized area of bone absorption at the posterior aspect of the lower part of the tibia, which was probably due to osteomyelitis. The patient was transferred to the Dermatology Center at Ashford General Hospital on Jan. 1, 1946, when I first saw him. There the observations were essentially the same as those made at Kennedy General Hospital. Roentgenograms of the chest showed the lungs to be normal, and sputum cultures disclosed no pathogenic organisms. The lesions of the face and leg continued to spread slowly. Pure cultures of B. dermatitidis were obtained from the lesions of the face and leg. The patient was treated with large doses of iodides, and in May 1946 the lesions were responding well to this treatment.



A, lesion of blastomycosis of the face; *B*, subcutaneous lesion of left ankle of same patient.

COMMENT

While Gilchrist's disease is limited almost entirely to the United States, the so-called European blastomycosis is observed in many parts of the world. When the latter disease affects the skin, it is often reported as Gilchrist's disease. It is possible to avoid this error in diagnosis by making cultures of the suspected organisms. In a direct smear from the lesions of each type of blastomycosis yeastlike cells with single buds are seen. When grown on blood agar at 37 C. the B. dermatitidis forms a pasty yeastlike culture and microscopically shows the budding forms only. On Sabouraud's agar at room temperature this organism forms a white fluffy colony. The Cryptococcus hominis of European blastomycosis never shows this type of mycelioid growth, but

remains yeastlike whether cultured at 37 C. or at room temperature. Other methods can be used to differentiate the organisms, but the cultural procedure is the most certain.

There are several interesting questions which arise in this case. The first question is whether the pneumonic disease was blastomycosis of the lungs, but the fact that no pathogenic fungi were isolated from the sputum tends to rule out blastomycotic involvement of the lungs. Also, the pulmonary lesions healed completely in four months with treatment with penicillin and sulfadiazine, while the cutaneous lesions persisted. The only observation in favor of a diagnosis of generalized blastomycosis was the subcutaneous lesion on the left ankle. The question whether the disease was localized or generalized blastomycosis is important in the consideration of prognosis. The latter form is nearly always fatal and the former rarely so.

Another question that arises is whether the patient contracted the disease in the United States or in England, many months previous to the appearance of the symptoms. According to the present knowledge of the disease this could not be so. The period of incubation of North American blastomycosis has been known to vary from one week to four months. Lewis and Hopper [3] stated that it is probably one to two weeks. This patient was in France for nearly ten months before he showed clinical signs of the disease.

Finally, the question arises as to whether the patient could have contracted the disease from a contaminated package from the United States. This is possible, but, if so, it would be the first recorded instance of transmission of blastomycosis in that manner in foreign commerce.

SUMMARY

The first proved case of North American blastomycosis from the European Continent is presented. The diagnosis in this case was established as North American blastomycosis, the micro-organism being differentiated from that of European blastomycosis by its characteristic culture.

9917 Euclid Avenue.

3. Lewis, G. M., and Hopper, M. E.: An Introduction to Medical Mycology, ed. 2, Chicago, The Year Book Publishers, Inc., 1943, p. 184.

Clinical Notes

VERRUCOUS SPOROTRICHOSIS

LESLIE M. SMITH, M.D. and H. D. GARRETT, M.D.
EL PASO, TEXAS

Lewis and Hopper[1] described six clinical types of sporotrichosis: (1) localized lymphangitic type, (2) disseminated subcutaneous type, (3) disseminated ulcerating type, (4) systemic type, (5) epidermal type and (6) a type with allergic lesions or sporotrichids.

To this classification we wish to add a seventh, namely, sporotrichotic dermatitis, a localized verrucous lesion involving both the epidermis and the corium, without subcutaneous infiltration, formation of deep nodules or abscesses, lymphangitic lesions, ulcerations, dissemination or systemic involvement.

One of us (L. M. S.)[2] has called attention to the varied characteristics which sporotrichosis may assume, emphasizing that one must expect to see cases of sporotrichosis which do not conform to the usual lymphangitic type, which is considered the classic picture of sporotrichosis.

The following case differs to such an extent from the usually accepted picture of the disease that it seems worthy of being recorded in the literature.

REPORT OF A CASE

Mrs. I. H., a Mexican housewife, aged about 40, consulted us on May 18, 1945 for a large verrucous lesion on the right cheek, the main portion of which was approximately 7 by 5 cm., with outlying satellite, superficial, pustular and verrucous lesions. The large area closely resembled blastomycosis, without deep infiltration and hardly as elevated as the usual lesion of blastomycosis. Thick material, composed of epithelial debris mixed with a small amount of pus, could be expressed from the crypts between the verrucous projections. There was no adenopathy, and the satellite lesions were only slightly infiltrated and did not suggest a lymphangitic dissemination but rather multiple autoinoculations. There was no history of exposure to thorns or shrubbery or of any other type of trauma.

The patient's general condition was excellent, and no evidence could be seen of lesions elsewhere. Curetted material and debris, obtained on pressure, failed to show any organisms on direct examination. Culture of this material, however, yielded a pure culture of a fungus which both grossly and on microscopic slide culture was typical of Sporotrichum.

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1. Lewis, G. M., and Hopper, M. E.: An Introduction to Medical Mycology, Chicago, The Year Book Publishers, Inc., 1939.

2. Smith, L. M.: Sporotrichosis: Report of Four Clinically Atypical Cases, South. M. J. **38**:505 (Aug.) 1945.

Fig. 1.—Verrucous sporotrichotic dermatitis.

Fig. 2.—Low power photomicrograph showing irregular acanthosis and cellular infiltration in the corium.

Histologic Data.—The epidermis showed moderate hyperkeratosis and decided irregular acanthosis, in certain areas approaching the picture of pseudoepitheliomatous hyperplasia with a tendency to whorl formation. The basal layer was intact except for one area where it was encroached on by a rather dense infiltrate beneath and the basal layer was not discernible. In the corium there was some vascular dilatation, though this feature was not so evident as has been reported by some observers. Throughout the corium and extending between the upper layer of fat cells there were large areas of dense infiltration, which consisted largely of lymphocytes with a generous admixture of plasma cells, connective tissue cells, some epithelioid cells and a few polymorphonuclear leukocytes. No miliary abscesses were seen, and no giant cells were present, although in several areas

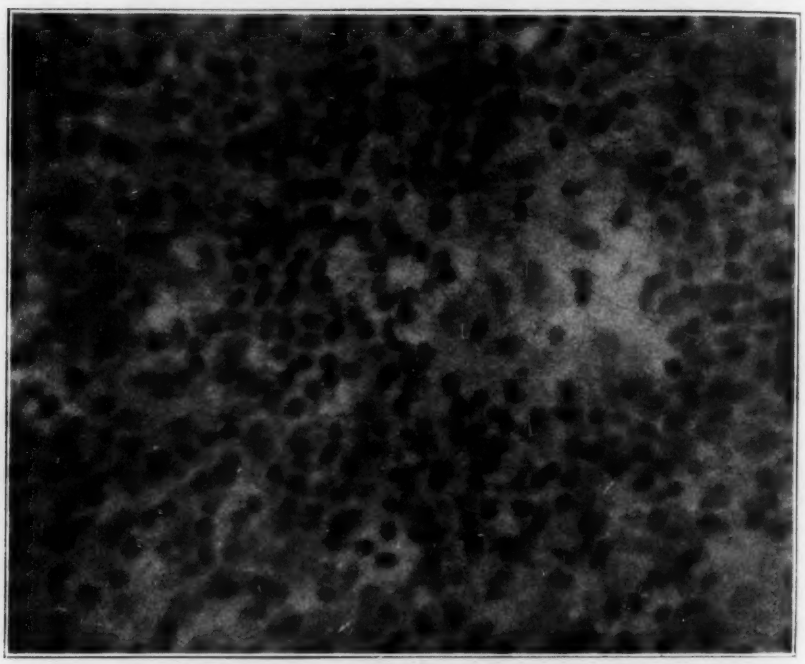


Fig. 3.—Higher power photomicrograph of cellular infiltrate in the corium.

there was an arrangement of epithelioid and round cells, somewhat suggesting the pattern of tubercles.

The lesions completely disappeared during the administration of strong solution of iodine, 15 to 45 drops daily, over a period of two months. The patient has recently been seen, approximately one year since the end of her treatment, and there has been no recurrence. Only a soft irregular slightly depressed scar remains.

SUMMARY

A case is presented of an unusual type of verrucous dermatitis due to Sporotrichum, which does not appear to conform to any of the types described in the usual classification of the disease.

931 First National Bank Building.

USE OF A SOCK AS AN ELBOW DRESSING

EDWARD F. CORSON, M.D.
PHILADELPHIA

In these days of scarcity of clothing the following suggestion may be received with reproach, but with appropriately worn-out cotton socks, which are of little value and with the principal holes in the toe, the procedure is not too wasteful and the method rather ingenious and useful. It was brought to my attention by a patient with psoriasis principally affecting the elbows. I have used it in a number of instances.

The region of the elbow is not easily bandanged by persons who do not have training in the art, and the usually tapered forearm encourages a poorly applied

Sock dressing.

dressing to slip down. This permits soilage of the clothing by secretions or "dirty" applications. If, however, a sock is drawn up the arm, in reverse to the usual fashion, through an opening formed by cutting off the toe end, and the foot of the sock is pulled above the elbow so that the heel of the sock receives the point of the elbow, it tends to stay in that position. A dressing of gauze pads, lint or cotton will be held snugly in place without rolled bandage or adhesive fastening. With a small amount of practice the patient becomes skilful at rolling the sock down part way, changing dressings and replacing the cover. For psoriasis of the region of the elbow, pyodermas, dermatitis, decubitus or irritation of the part by bed linen, as frequently noted in bed patients, the sock dressing has given satisfaction.

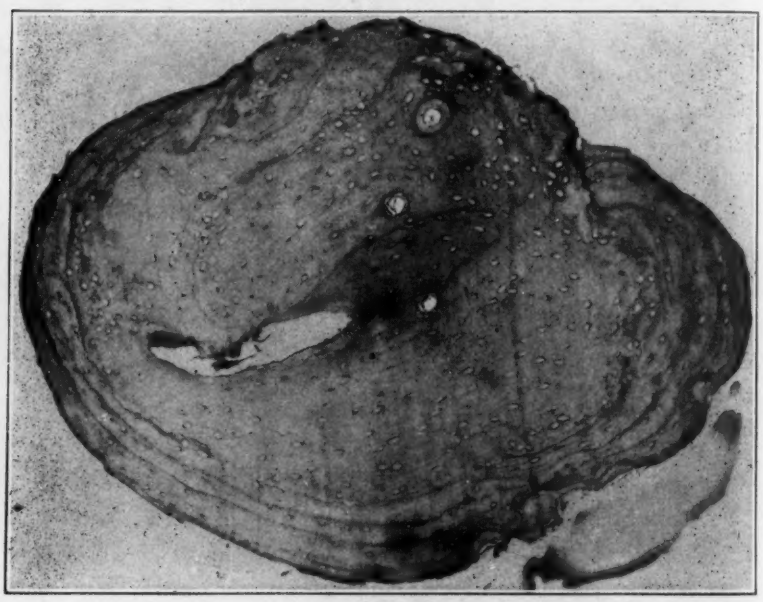
Sections of hosiery are commonly employed for other parts of the extremities than those for which they were originally intended, but when over the front of the elbow they are more likely to roll up and form irritating folds.

METAPLASIA OF BONE

Report of a Case

MAURICE J. COSTELLO, M.D.
NEW YORK

An unmarried white woman aged 53 requested the removal of a number of milia and milium-like lesions of the face. The lesions occurred singly, on the lower half of the center of the forehead, on the cheeks, the nose and the sides of the chin. Some of them appeared to be slightly elevated, pinhead-sized to match-



Osteoblasts imbedded within an osseous matrix (low power magnification).

head-sized, nonpigmented moles, but they were hard to the touch. A grating sensation was experienced when the pointed bistoury was used to incise the skin as a preliminary step in the removal of the content of the lesions, which "popped out" in one piece. The largest of about a dozen lesions was half lentil sized, stony hard and shaped like a miniature cauliflower. The milia were of varying degrees of hardness, from what would be expected to a degree approaching the aforementioned description. This gave the impression that the lesions showing metaplasia of bone began as milia.

A specimen studied by Dr. Fred D. Weidman showed that "the epidermis had become detached from the rest of the specimen, and none of the architecture of the skin was submitted for study. What there was had the structure of bone, with typical osteoblasts embedded within a pink osseous matrix. Calcification appeared only in the form of shreds of blue granules which were patterned as

though they might be surrounding, concentrically, certain spaces which occupied the general osteoid matrix. The structure of genuine bone marrow was not identifiable within these spaces. At most, they contained only a few dilated blood vessels together with fatty areolar tissue. Inasmuch as marrow tissue did not occupy the spaces mentioned and calcification was developed so poorly, it could be stated only that this tissue was osteoid. Such tissue can occur as an expression of metaplasia of bone within old cicatrices or other residua of ancient processes. These observations agree with the circumstances reported clinically."

A case similar to this one has been reported by J. G. Hopkins.[1]

140 East Fifty-Fourth Street.

1. Hopkins, J. G.: Multiple Miliary Osteomas of Face, Arch. Dermat. & Syph. **18**:706 (Nov.) 1928.

SMALLPOX VACCINATION IN RELATION TO VIRUS DISEASE

HERMAN SHARLIT, M.D.
NEW YORK

A physician has had recurrent herpes simplex for nineteen years. For the first twelve years it was localized to the shaft of the penis; for the last seven, to the right buttock. The attacks never occurred more often than two or three times a year. The last attack subsided April 5, 1947. On April 13 this physician began vaccinating patients. (The Department of Health of New York City recommended that all the population receive cowpox vaccination at once.) Four days later this physician had another attack of herpes on the same buttock, this lesion being about 1 inch (2.5 cm.) from the location of the last. The physician himself had not been vaccinated at this time.

It is impossible for one giving many vaccinations to avoid receiving some of the vaccine lymph on his fingers, without local reaction. It is statistically reasonable, in view of this nineteen year history, to believe that the recurrence of these two attacks of herpes in quick succession was not a coincidence. One may accept the exposure to vaccine lymph as causally related to the last attack.

I need not indulge in obvious comment in this communication, but I would call attention to the opportunity now offered the physicians of New York city to make many helpful observations on the clinical influences of cowpox vaccination on patients with chronic virus infections.

Observation from the New York Vaccination Campaign.

COMEDOS FOLLOWING ROENTGEN RAY THERAPY

SAMUEL M. BLUEFARB, M.D.
CHICAGO

The appearance of comedos in a zone surrounding the scar following roentgen therapy for an epithelioma of the face has recently been observed. The case is the first to be encountered out of several hundred cases of epithelioma treated by a similar technic in the dermatology clinic.

From the Department of Dermatology, Northwestern University Medical School, Edward A. Oliver, M.D., Chairman.

The patient, a 63 year old man, had an epithelioma on the cheek (fig., *A*), which on histologic examination was found to be of the mixed cell type. He was treated with roentgen rays, receiving 2,160 r once each week for three weeks. The site healed within the course of eight weeks, and when examined several weeks later there was an atrophic scar with slight depigmentation, around which blackish horny lesions were arranged in a concentric zone (fig., *B*). On compression with a comedo extractor, each of the horny plugs was found to be a

Fig. 1.—*A*, mixed cell epithelioma of the face. *B*, comedos surrounding the roentgen ray scar.

comedo. In the section of the illustration showing the lesion as it was before treatment, there is no evidence of comedos.

This lesion constitutes a clinical curiosity unique in my experience and has no other significance. I have been unable to find a report of any similar case in the literature which is available to me.

Ormsby and Montgomery [1] stated that the comedo is due to hyperkeratosis occurring about the neck of the follicle, causing retention of the fatty material which should ordinarily be thrown off. It is believed that irritation induced by the microbacillus of Unna and Sabouraud is usually the cause of hyperkeratosis. Others have associated the formation of comedos with folliculitis resulting from infection. At times, as in some cases of grouped comedos, the irritant is found in chemicals such as oils (e. g., Brilliantine or camphorated oil). Becker and Obermayer [2] stated that comedos are occasionally seen about the eyelids in elderly persons and must be interpreted as senile phenomena. In fact, it is most likely that any type of reflex or local disturbance which would tend to increase the activity of the sebaceous glands may lead to the formation of comedos. The most frequent form is that seen associated with acne vulgaris.

These facts are pertinent in this case: 1. The patient was beyond the age at which acne occurs. 2. There was no evidence of comedos before roentgen therapy. 3. The comedos appeared in the zone beyond the healed scar. Therefore, it is assumed that the comedos in this case were due to an irritation of the follicles of the sebaceous glands immediately surrounding the roentgen ray scar, and it is presumed that it represents a compensatory hypertrophy of the sebaceous apparatus.

30 North Michigan Avenue.

1. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, Philadelphia, Lea & Febiger, 1943, p. 1215.

2. Becker, S. W., and Obermayer, M.: Modern Dermatology and Syphilology, Philadelphia, J. B. Lippincott Company, 1940, p. 521.

RESULTS OF REPEATED EPILATION WITH ROENTGEN RAYS IN TINEA TONSURANS

H. H. HAZEN, M.D.
WASHINGTON, D. C.

In the past thirty years some 500 children with tinea tonsurans have been treated with the roentgen ray in the office. The standard five point exposure method has usually been employed,[1] although occasionally a four point exposure system has been used. Certain of these children had more than one treatment, and as there are certain hazards connected with this it seems wise to point them out, since the disease has become so prevalent over much of the country.

Thirty of the children had two roentgen ray epilations, and in every instance the regrowth of hair was satisfactory. The interval between the two treatments was in each case not less than three months. The second treatments were necessary because of reinfections, which occurred in orphan asylums of some type. Five Negro boys, inmates of the City Orphanage at Blue Plains, were each treated three times within fifteen months. This was due to error on the part of a too zealous institutional attendant. The boys varied in age from 8 to 11 years, and all were affected by the human type of ringworm. Following the second epilation the regrowth of hair was satisfactory, as in MacKee's [2] experience, but after

1. Hazen, H. H.: X-Ray Treatment of Tinea Tonsurans, J. Cutan. Dis. **37**: 307, 1919.

2. MacKee, G. M.: X-Rays and Radium in the Treatment of Diseases of the Skin, ed. 3, Philadelphia, Lea & Febiger, 1938, p. 469.

the third treatment the hair did not reappear for at least three months, and then it was dry and uniformly scanty. As nearly as could be estimated, between one third and one half of the hair reappeared. Many of the hairs showed alternate rings of white and black, sometimes as many as six to a hair, about half an inch (1.27 cm.) in length. Some two years later 3 of these boys were seen again, and none had shown any improvement. It is worthy of note that all patients were treated with the same apparatus and by the same operator, and that they were not all treated on the same day.

Judging from these observations it would seem that while two standard roentgen ray epilations are perfectly safe, a third should never be done.

1911 R Street, N. W.

PILI TORTI

Report of a Case

WILLIAM M. SISKIND, M.D.
NEW YORK

Pili torti is a rare disease of the hair; the pathogenesis is unknown, and the treatment is unsatisfactory. Pili torti is usually considered a congenital disease. In Ormsby and Mitchell's [1] case the disease had been present at birth, with a slight growth of hair when the child was 14 months; they stressed the resemblance to monilethrix. In Ronchese's [2] case it was also of congenital origin, other members of the family being similarly affected. His patient improved with the application of hydrous wool fat to the scalp.

Clarke and Glicksberg [3] reported a case of a 14 year old boy who had been completely without hair until 5 years of age. Investigation of the endocrine system revealed no abnormalities. The association with keratosis pilaris and also monilethrix has been reported.

REPORT OF A CASE

R. Z.,[4] aged 17, presented herself in January 1946, complaining of extreme shortness and brittleness of the hair of the scalp, with loss of hair in several areas.

History.—The patient had a normal birth and development, with no serious diseases of childhood until 1940, when she had a severe attack of scarlet fever. After this she noticed that her hair was brittle, did not grow to its former length and had lost its luster. Small patches of baldness also developed on the top and sides of the head. She has not cut her hair since her illness six years previous to the time of consultation.

She has one brother, whose hair is curly but grows normally. Her father and mother have no disease of the hair.

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1. Ormsby, O. S., and Mitchell, J. H.: Atrophia Pilorum Monilethrix, Arch. Dermat. & Syph. **10**:393-394 (Sept.) 1924.

2. Ronchese, F.: Twisted Hairs (Pili Torti), Arch. Dermat. & Syph. **26**:98-109 (July) 1932.

3. Clarke, G. E., and Glicksberg, E. L.: Pili Torti: Report of Case, Arch. Dermat. & Syph. **43**:836-838 (May) 1941.

4. This patient was presented before Manhattan Dermatological Society and reported by Wise, F.: A Case for Diagnosis (Pili Torti), Arch. Dermat. & Syph. **45**:1183-1184 (June) 1942.

Examination.—The girl was normally built and developed. No abnormalities were found except for the scalp and the presence of keratosis pilaris of both arms and thighs.

The temporal, frontal and vertex areas of the scalp were mainly involved. The hair in these regions was short and lusterless and clung closely to the scalp. Throughout the affected areas there were small patches of partial alopecia. The back of the head was not affected, the hair being long and wavy. This hair was combed up over the top as a covering for the involved areas. The length of the diseased hairs varied from ¼ to ½ inch (0.64 to 1.27 cm.), and the hair was decidedly curled and twisted.

Microscopic examination proved the diseased hairs to be twisted on the long axis of the shaft at regular intervals, the hair shaft between the twists being normal in appearance. The superficial resemblance to monilethrix was striking, but on close examination it was seen that at the constricted points the hair was twisted completely on its axis.

Treatment.—Because of the presence of keratosis pilaris and the known influence of large doses of vitamin A on it, she was given 200,000 U. S. P. units of this vitamin daily. At the end of three months the improvement was striking. The keratosis pilaris had completely cleared up, and the alopecia had greatly improved. There was a regrowth of new hair, and the affected hair grew out longer, so that the average length of the hair in the area most involved now measured 2½ to 3 inches (6 to 7.6 cm.).

SUMMARY

A case of pili torti is reported. The disease, from all available evidence of the history, started after a severe attack of scarlet fever. Treatment by high doses of vitamin A was found to be effective for this rare anomaly of the hair.

152 East One Hundred and Seventy-Ninth Street.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

Lewis B. Robinson, M.D., *Chairman*

Samuel M. Peck, M.D., *Secretary*

Nov. 12, 1945

Papulonecrotic Tuberculid. Presented by Dr. Frederick Reiss.

F. C., a woman aged 33, was first observed in the dermatologic clinic of the New York Hospital on Oct. 21, 1937 with erythema induratum, which subsequently healed. At that time the patient was being treated for advanced pulmonary tuberculosis with bilateral pneumothorax. She returned in September 1945 with lesions on the lobe of the right ear and the scalp, of six months' duration.

On the lobe of the right ear there are two depressed, hyperpigmented scars and three or four inflamed papules with a necrotic top. Several similar lesions are scattered over the scalp. There are no changes on the extremities.

Roentgenographic examination on Oct. 5, 1945 gave evidence of residual pleural thickening throughout both sides of the thorax, more noticeable in the apexes, from reexpansion after pneumothorax, and a fibrocalcific tuberculous process in the upper lobe of the right lung and a few fibrous scars in the upper lobe of the left lung.

The erythrocytic sedimentation rate was 10 mm. in one hour. A smear of the sputum was negative for acid-fast bacilli. A test with old tuberculin in a dilution of 1:1,000 gave a necrotic papule in forty-eight hours, with a surrounding erythematous area of 6 cm. The Wassermann reaction of the blood was negative.

Biopsy showed the epidermis to be thick and flattened, disintegrated in some places and replaced by a scab of polymorphonuclear leukocytes. The corium was dense and fibrous and was invaded by a large number of leukocytes, most of which were polymorphonuclear forms. Part of the collagenous tissue had undergone coagulation necrosis, but there was no sign of tuberculoid structure. It was felt that this stage of the histologic changes might represent an early acute, nonspecific reaction to tuberculotoxins.

DISCUSSION

Dr. E. W. Abramowitz: From the appearance of the lesions on the scalp, one would suspect lupus erythematosus. The lesion on the ear may be a giant-sized papulonecrotic tuberculid. I have seen such a lesion, although it is unusual. The patient will bear watching for other signs of lupus erythematosus or papulonecrotic tuberculid, and I believe that another biopsy is indicated.

Dr. Frederick Reiss: I feel exactly as Dr. Abramowitz does. If he had seen the patient eight weeks ago, he would have been confronted with the same puzzle. I still think there are cases in which papulonecrotic tuberculid follows the course in this case. However, the lesions on the scalp are somewhat suggestive of lupus erythematosus.

Scleroderma. Presented by DR. MABEL SILVERBERG.

M. H., a girl aged 9, was first observed in the dermatologic clinic of the New York Hospital on Dec. 22, 1943. The child had had chickenpox but no other diseases. Four years ago it was noted on routine examination that the patient's face was somewhat puffy. One year later the right cheek appeared swollen and bluish red. The area was sharply demarcated. The left cheek also appeared somewhat red and puffy at this time. Six months later the right lower eyelid, the right side of the nose, the right cheek and the right temporal region were distinctly indurated and showed areas of an ivory white color. The lashes of the right lower lid had fallen out.

The skin of the face on the right side in the temporal area and over the right cheek, the right lower eyelid and the right side of the nose is depressed and hidebound and varies in color from an ivory white to a mottled tan. There are three areas of pronounced induration the size of a quarter. Alopecia of the right lower lid is present. The mottled brownish discoloration extends over the chin, which, however, is not indurated.

The urine was normal on frequent examinations. The blood count on Dec. 14, 1943 showed 12 Gm. of hemoglobin per hundred cubic centimeters, 4,580,000 red cells and 7,800 white cells, with 50 per cent lymphocytes, 45 per cent polymorphonuclear leukocytes, 3 per cent eosinophils and 2 per cent monocytes. The count on Aug. 21, 1944 showed 12 Gm. of hemoglobin, 4,480,000 red cells and 6,000 white cells, with 72 per cent lymphocytes, 25 per cent polymorphonuclear leukocytes, 2 per cent eosinophils and 1 per cent monocytes. The Wassermann reaction of the blood was negative on Oct. 5, 1942. On Sept. 5, 1944 the Wassermann reaction of the blood was negative and the Mazzini reaction doubtful. The serum calcium was 12 mg. per hundred cubic centimeters on Oct. 6, 1944. Roentgenograms of the sinuses and teeth were normal.

Treatment has consisted of daily massage with hydrous wool fat. The patient is presented for therapeutic suggestions.

DISCUSSION

DR. EUGENE T. BERNSTEIN: I think the case is one of hemiatrophy facialis, a disease based on trophic disturbances affecting the muscles, tissues and bony structures. Scleroderma-like changes are also seen in this case, but the entire half of the face is in a state of atrophy. There is also involvement of the bony structure. There is a spot on the eyelid which one cannot pick up with the fingers, but otherwise the skin is freely movable. I think it is justifiable to place this case in the category of hemiatrophy facialis.

DR. FRANK VERO: I agree with Dr. Bernstein in the diagnosis of hemiatrophy, which is often associated with scleroderma.

DR. SAMUEL M. PECK: I also agree with Dr. Bernstein that there is not only a cutaneous atrophy but also involvement of the underlying subcutaneous tissue, as well as the muscles, on that side. The disease was described by Kartagener and myself in 1928 (*Dermat. Ztschr.* **52**:81, 1928). In the case we reported there were both hyperpigmentation and depigmentation, as well as loss of hair. Later, I saw 2 other cases in which the lesions were of the same type, 1 in a male and the other in a female. The results of treatment in all my cases were very poor.

DR. FRED WISE: Does the case which Dr. Peck has just described come under the same category as *coup de sabre?*

DR. MABEL SILVERBERG: I am not sure whether there is atrophy of bone in the present case, although there appears to be. I first saw the child in the edematous stage, when there was no atrophy, then the eyelid became involved with typical scleroderma. There was no doubt of scleroderma at the onset, and atrophy of the bone, if present, developed later.

Scleroderma; Tropic Ulcers; Calcified Ganglion of Tendon Sheath.
Presented by DR. MABEL SILVERBERG.

M. T., a man aged 56, Jewish, born in Austria, first came to the New York Hospital on June 21, 1945. Stiffness of the skin had gradually become more noticeable during the preceding eight years, although he was not aware that his condition differed from the normal. His reason for consulting a physician was the pain from ulcers on the outer side of each foot. These ulcers were treated by his physician with local medication and finally with fulguration. Foot baths were prescribed but did not help. Some healing has resulted from the local use of penicillin ointment. He states that cold weather does not bother him.

The face and extremities show hidebound skin, with absence of wrinkling and considerable immobility. Perforating ulcers are present on the outer side of each foot. A cystic lesion on the back of the left hand (ganglion of a tendon sheath?) is hard to the touch and is thought to be partially calcified. Scattered over the thighs and other parts of the body are brown maculopapules. Histologic section of one of these lesions revealed typical sclerodermic changes. The Mazzini test gave a negative reaction. The basal metabolic rate was —2 per cent.

DISCUSSION

DR. FRED WISE: My associates and I have used dihydrotachysterol in our clinic for the past five years, without obtaining any definite responses that we could ascribe to its use. Dr. George C. Andrews, at the last meeting of the New York Dermatological Society, mentioned 2 cases of progressive scleroderma treated with injections of penicillin, with pronounced improvement. Since dihydrotachysterol is a relatively harmless drug, it should be given a trial in cases of progressive scleroderma.

DR. SAMUEL M. PECK: When dihydrotachysterol was first suggested as a therapeutic agent for scleroderma, it was eagerly seized on by most dermatologists. However, it was soon realized that, although some benefit was to be derived from its use in the edematous stage of the disease, the drug, as was to be expected, had no effect on the atrophic end stage. Neither has it been my experience that this drug is able to halt the course of progressive scleroderma. One must be cautious in evaluating the results of therapy of scleroderma in the edematous stage. This stage tends to run its course, and at the end of this period, just before the more serious atrophic stage becomes manifest, the patient actually feels better; if the hand is involved, there is ability to move the fingers more easily. This apparent improvement might lead to the erroneous conclusion that the course of the disease is influenced by whatever therapy is being carried out at that time. Unless one is to conclude that scleroderma is due to a focus of infection or is an infectious process, I cannot understand why penicillin should be successful in treatment of this disease. In cases of scleroderma with dermatomyositis one might have better results with penicillin, for it has been my impression that the latter process was infectious in character.

DR. EUGENE T. BERNSTEIN: I presented before this society a case of generalized scleroderma in which excellent subsidence of all sclerodermatous features was obtained under treatment with dihydrotachysterol. I also presented a case before the clinic at Mount Sinai Hospital, a report of which was published in *The Journal of the American Medical Association* (**140**:570 [March 2] 1946). Dr. Wise, in his discussion, stated that this was the first case he had seen in which dihydrotachysterol was efficacious to such an extent, with complete recession of all symptoms.

DR. FRANK VERO: It is unusual to see such extensive changes involving the feet and toes. In a large series of cases at the Presbyterian Hospital, I do not recall one in which there were such pronounced changes on the feet, although one may see hidebound skin on the legs and ankles. This patient presents typical acrosclerosis of the feet, but I am not certain that the lesions on the thighs are morphea unless they are in the stage of involution. I palpated several lesions and could not feel the typical hardness. As to therapy, I have to disagree with the good results from use of the drug (dihydrotachysterol) mentioned by Dr. Bernstein. I have seen a number of patients with scleroderma treated with dihydrotachysterol with no improvement whatever. Dr. Peck is correct as to the difficulty of evaluating any therapy for scleroderma. I have observed several patients who have benefited greatly from a change to a warm climate. Two patients, 1 with diffuse and 1 with progressive scleroderma, went to Florida during the winter and returned with no progression of the disease whatever. I think that massage, diathermy and possibly neostigmine will be of aid in Dr. Silverberg's case. I have obtained good results in some cases from injections of neostigmine methylsulfate and from oral administration of neostigmine bromide.

DR. FRED WISE: Dr. Peck's point is well taken; dermatomyositis, which is probably an infectious disease, is frequently associated with scleroderma-like changes, and it is possible that penicillin might be operative in combating the assumed infectious agent and might also benefit the associated scleroderma.

DR. E. W. ABRAMOWITZ: This patient has atrophy of the skin; the venules are prominent, and, although there is no terminal distal ulceration, ulcerations are present on the heels. He probably has some degree of peripheral vascular disease. He has scattered macular atrophic patches on the legs. In addition, there is a calcareous synovial ganglion on the wrist, and he has acne varioliformis on the scalp. I think the diagnosis of scleroderma should be held in abeyance. In the meantime, baking and massage with oral administration of neostigmine bromide (15 mg. three times a day) might be tried.

DR. MABEL SILVERBERG: Unlike the other patient, I have seen this patient only once.

A Case for Diagnosis (Melanoderma?). Presented by DR. FREDERICK REISS.

M. J., a Negro woman aged 38, was first observed in the dermatologic clinic, New York Hospital on Sept. 27, 1945, complaining of an eruption on the face of one year's duration. Small lesions, about 1 cm. in diameter, appeared on both cheeks. At the onset these were slightly itchy, dusky gray and nonscaling. At times they became reddish, and small "pimples and blisters" appeared and disappeared as the eruption spread.

On both cheeks and on the forehead there are several hyperkeratotic follicles, which become slightly confluent, forming small, discrete patches, which are partly reticular. Some of the papules have a violaceous color. There is no atrophy.

The Mazzini test was negative on Sept. 27, 1945. A blood count on October 2 showed: hemoglobin content 9.7 Gm. per hundred cubic centimeters, 3,800,000 red blood cells, normal platelets, and 6,800 white blood cells, with 50 per cent lymphocytes, 48 per cent polymorphonuclear leukocytes, 2 per cent eosinophils and no monocytes or basophils. A blood smear showed slight achromia. The corrected sedimentation index was 0.3; the total fall was 0.5 mm. in one hour; the red cell volume was 38 per cent.

Histologic examination showed a moderate amount of parakeratosis and hyperkeratosis, affecting especially the follicular orifices. There were thickening of the epidermis and moderately copious sleeves of lymphocytes about the vessels of the derma and in the neighborhood of the hair follicles. Melanophores were not present in the cutis. There was no basophilic degeneration.

DISCUSSION

DR. BEATRICE M. KESTEN: I do not know what this eruption is. It might be well for us to have a clinic and present the variety of pigmentations seen in the Negro skin. We could then clear up the terminology.

DR. SAMUEL M. PECK: There is one objection to the diagnosis of pigmentary dermatosis in this case, and that is the fact that one is dealing with a colored skin. In an inflammatory process a colored skin acts differently from a white skin; i. e., it becomes pigmented or depigmented. There seems to be atrophy in some of the lesions, but I should hesitate to label the disease as pigmentary dermatosis. Even acne will often cause pigmentation in a colored skin.

DR. EUGENE T. BERNSTEIN: I think a diagnosis of Riehl's melanosis should be established here. This dermatosis affects the face in exactly the locations seen in this case. I think poikiloderma occurs more frequently on the neck.

DR. FREDERICK REISS: I believe that in Riehl's melanosis the pigment is more diffuse, and not lichenoid, as in this case. I am not quite convinced that this case represents the Hoffmann-Habermann type of melanosis, but that is the most nearly suitable diagnosis that I could suggest.

A Case for Diagnosis (Parapsoriasis?). Presented by DR. THOMAS N. GRAHAM.

E. K., a white woman aged 66, was first seen in the dermatologic clinic of New York Hospital on Dec. 1, 1941, complaining of a generalized, slightly scaly eruption, with very little itching, which had been present for four years. The histologic diagnosis at that time was "cutaneous lesion resembling both parapsoriasis and pityriasis rosea." The patient returned on Oct. 10, 1945, at which time her eruption was essentially the same as on her previous visit.

Most of the cutaneous surface shows an erythematous, macular eruption, with "branny" scaling. On the anterior surface of the chest and neck there are dilated blood vessels, which suggest poikiloderma vasculare atrophicans. There are also a number of violaceous papules on the neck. Numerous erythematous, small, follicular papules occur on the arms.

The Mazzini test of the blood gave a negative reaction on Aug. 9, 1945. The blood chemistry was essentially normal. The urine was normal. A blood count showed 10.5 Gm. of hemoglobin, per hundred cubic centimeters, 3,200,000 red cells, normal platelets and 5,000 white cells, with 59 per cent polymorphonuclear leukocytes, mature form, 6 per cent band cells, 30 per cent lymphocytes, 2 per cent monocytes, 3 per cent eosinophils and no basophils.

Biopsy showed general flattening and thickening of the epidermis, a well marked, but somewhat interrupted, granular layer and a fibrous and thickened derma with sleeves of lymphocytes about the vessels. There was rather conspicuous cavitation of the cells of the rete malpighii, but no parakeratosis was noted and little keratosis. The picture was thoroughly equivocal; in the absence of parakeratosis, it was more similar to that of parapsoriasis *en plaque*. The basal layer was scarcely recognizable, a characteristic of parapsoriasis; so the diagnosis is questionable parapsoriasis *en plaque*.

DISCUSSION

DR. FRED WISE: The reticulated eruption gives the impression of parakeratosis variegata, described by Unna, Santi and Pollitzer.

DR. EUGENE T. BERNSTEIN: I suggest the diagnosis of seborrheic dermatitis. The patient has scaliness and dandruff of the scalp. I do not think the eruption is parapsoriasis.

Tinea Capitis Due to Microsporon Audouini. Presented by DR. MARGARET KLUMPP and DR. FREDERICK REISS.

M. P., a married white woman aged 32, was first observed in the dermatologic clinic of the New York Hospital on Feb. 23, 1944. The patient had two small children attending the clinic for treatment of M. audouini infection of the scalp. She called our attention to her scalp because of itching. Examination with Wood's light showed several patches of fluorescent hairs scattered over the scalp, and cultures revealed M. audouini. The patient had had alopecia areata several years ago, with no return of the hair. She had smooth, noninflammatory areas of alopecia involving chiefly the posterior hair line and extending upward about 2 inches (5 cm.) from this level. In addition, there was complete loss of the eyebrows and eyelashes. Otherwise, there was nothing unusual in the patient's history or examination.

Manual epilation and application of 10 per cent ammoniated mercury U. S. P. proved of no avail, and it was decided to administer estrogen by mouth. It was given in the form of mestilbol N. N.R. ("monomestrol tablets") 2 mg. daily, in the second half of the menstrual cycle, the dose being later increased to 2.5 mg. a day. This medication was repeated during each cycle from May through July 1944. Thereafter, estrogenic substances N. N. R. ("premarin"), 2 tablets (0.63 mg. each) daily, was given from July through September 1944. During this time there was no improvement in the status of the infection. Subsequently, local epilation with roentgen irradiation was performed, and the affected areas treated with 6 per cent sulfur and 3 per cent salicylic acid. Since it was assumed that the oral medication with estrogen preparations could not raise the hormone level of the blood to such an extent as to produce an adequate concentration in the affected areas, it was considered advisable to apply stilbestrol, 0.04 per cent in an aerosol base, locally. After this treatment the infected hairs became loose and could easily be pulled out, whereas prior to the treatment this had been almost impossible without breaking the hair. The infected area also became smaller, but many infected hairs were still present, as judged by their fluorescence under Wood's light. It may be added that local application of methyl testosterone, 5 mg. daily, was made for about two weeks, without appreciable benefit. For another two weeks thyroxin, 0.01 per cent in an aerosol base, was applied, resulting only in easier manual epilation. At present there are still many foci of fluorescent hair.

Cultures of material from the scalp yielded M. audouini. The urine was normal. The Mazzini reaction of the blood was negative. The basal metabolic rate was —8 per cent. The cholesterol of the blood was 318 mg. per hundred cubic centimeters. Vaginal smears showed a "normal cycle," as read by Dr. E. Shorr.

DISCUSSION

DR. MARION B. SULZBERGER: It is an understatement to say that this infection is relatively rare. It is most unusual to find a proved case of infection of the scalp with M. audouini in an adult. I do not recall having seen such a case and have heard of only 1 or 2 instances. Its presence in this case means that the woman has an anomaly which makes her scalp and hair like that of a child with respect to susceptibility to infection with M. audouini. While it appears logical to make these therapeutic approaches with endocrine products, the treatment has had notable lack of success in children. Androgens and estrogens have been administered, both systemically and locally, in almost every form, natural and synthetic, to the point of producing artificial puberty; and one may say that none of these procedures has proved of any value. While there is a remote possibility that an adult might react differently from a child, the results reported indicate that here, too, administration of these hormones has failed. I hope I am not "jumping the gun" by telling you that Dr. Stephan Rothman, of Chicago, has been making studies on the nature of the difference between adults' and children's hair, which will shortly be published. Dr. Rothman has isolated a factor from adults' hair which kills M. audouini and which is not present in children's hair before puberty.

DR. BEATRICE M. KESTEN: I wonder whether we are not simply accepting this idea of the rarity of fungous infections in adults. Perhaps if one were to examine the mothers who come in with infected children, more cases of tinea capitis would be found in adults.

DR. SAMUEL M. PECK: I should like to subscribe to Dr. Kesten's suggestion. I have seen girls and boys past the age of puberty, 16 years or older, who acquired their infections with M. audouini before puberty and still showed persistent infection of the scalp. C. H. Danforth, in his monograph on "Hair," published in 1925, pointed out that the scalp during the first few years of childhood becomes coarser and the average diameter of the hairs approaches that of the adult hair. Most of the coarse hairs of young children are without a medulla, although an occasional hair with an interrupted, or even continuous, medulla may be found from an early age. After puberty the number of hairs with a medulla increases, but in general there are many hairs, even in old age, which still lack the medulla. Consequently, if one were to stick closely to the definition of a terminal hair as one containing a medulla, it would be necessary to regard a considerable part of the hair of the head as transitional. If the structure of the adult hair is the reason that adults seem to be resistant to infection with M. audouini, perhaps it is these transitional hairs, still retaining the childhood structure, which, if they are in predominance, would account for the persistence of some of the postpuberty infections. However, that is not my conception of why adults seem to be resistant to infections of the scalp with M. audouini. My collaborators and I, as well as others, have pointed out that the sweat glands play an important role in fungous disease by contributing to the secretion of substances which are fungistatic. Perhaps in adult life the glands of the scalp also secrete a substance which helps to control infections of the scalp. I was interested in Dr. Sulzberger's comment that Rothman has isolated from adult hair a substance which is lacking in the hair of children and which may account

for the resistance to infection of adult hair. However, I wonder whether Dr. Sulzberger recalls the experiments in the Zurich clinic, where it was found that culture mediums made from adult hair readily served as a medium for fungi, including M. audouini. Such observations support my contention that the secretions of the glands play a role in preventing infection rather than some substance possibly contained in the hairs themselves.

DR. MARION B. SULZBERGER: With regard to Dr. Kesten's suggestion of the likelihood of finding fungous infections in adults exposed to infected children: Even if that were the case, I am sure that persistent infection is rare in an adult. To be sure, occult and sporadic subclinical infections of adults may be more common than is supposed. I remember the experiments at Zurich mentioned by Dr. Peck. However, I found there that M. audouini grew very poorly on adult hair in vitro. The fungous inoculations on adult hairs formed the *fuseau*, a spore regarded as indicative of poor and inhibited growth.

DR. HERMAN GOODMAN: An alkaline reaction is held to favor the microsporon infection of the scalp in children. Free acid sweating seems to produce improvement in the tinea. Adults show a p_H on the acid side. This served as a clue to the failure of many adults to become infected with the microsporon. Acid rinses were proposed and utilized for care of the scalp, the lemon rinse being a favorite.

It would be interesting if it were possible to determine the p_H balance of the scalp of preadolescent and postadolescent persons. The present modes of recording the p_H do not reflect the actual condition. Those available give only the p_H of the aqueous phase of an emulsion. No apparatus is yet available to give direct readings of the p_H of the oil side of an emulsion. The covering of the skin has the sweat-water phase and oil phase, representing the products of the sebaceous sacs. Perutz (Die Pharmakologie der Haut, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer 1932, vol. 5, pt. 1) cited some of the work in this field. Other pertinent references are: Beeler: J. Am. Pharm. A. (Practical Pharmacy Edition) **3**:233, 1942 and Harry, R. G.: Hydrogen Ion Concentration in Therapeutic Bases, Brit. J. Dermat. **54**:1, 1942.

Incidentally, will the presenters explain what was to be expected by offering hormone therapy? How, theoretically, would it affect the scalp? What safeguards were utilized to prevent undue influence of the hormone on the patient's normal sexual activities.

DR. HELEN O. CURTH: This woman also has alopecia areata. She still has spots on the occiput and shows loss of the eyebrows. I wonder whether this preceding and accompanying disease of the scalp could not have caused some strange response to the infection with M. audouini.

DR. FRANK VERO: One of my colleagues informed me that he has used electrolysis with good results for the removal of residual hair which still showed fluorescence. With reference to the comments of Dr. Kesten and Dr. Sulzberger on examination with the Wood light, I see every afternoon in the clinic children sent from the board of health for whom a diagnosis of tinea capitis could not have been made clinically. There are no signs of any inflammatory changes, broken-off hair or bald spots, but examination with the Wood light shows fluorescence. I wonder whether the increase in the number of cases of tinea, said to be of epidemic proportions, is not due to discovery of more cases through application of the Wood light.

DR. SAMUEL M. PECK: It is no longer valid to doubt the ease of diagnosis of fungous infection of the hair by means of the Wood light. It has been shown in thousands of cases that an experienced observer can detect an infection of the

scalp with M. audouini in almost 100 per cent of cases provided the hair above the surface of the scalp is infected with the organism. The fluorescence is so specific that one could not fail to differentiate between fluorescence due to the organism and fluorescence due to something else.

DR. FRANK VERO: In answer to Dr. Peck, I should like to add that in the cases of tinea capitis I have seen at the department of mycology of the Vanderbilt Clinic in which there was no clinical evidence of infection examination showed a typical fluorescence of the hair, cultures yielded M. audouini and the hairs had to be epilated.

DR. MARION B. SULZBERGER: Dr. Vero means that many subclinical cases of true infection with M. audouini could not be recognized until the Wood light was introduced. He means that the correct diagnosis is being made more and more often since the advent of the Wood light and that one is now able for the first time to gain an accurate idea of the number of cases of subclinical infection with this fungus.

DR. EUGENE T. BERNSTEIN: L. M. Smith, of El Paso, Texas, inaugurated the idea of hastening puberty as a physiologic defense mechanism against the growth of M. audouini. Some of my colleagues have been obsessed with the idea of giving children such hormones as testosterone and estrogen. I think it is an intrusion into a child's being to give estrogens, for that changes the entire glandular apparatus.

DR. FREDERICK REISS: We assumed that injected estrogen could not reach the same level in the skin as that obtained with topical applications; so the substances were applied directly to the affected areas. We later changed to androgens. Under the treatment outlined, the infection was reduced to a certain extent. When the lesions did not completely disappear, thyroxin was given, on the assumption that there was a chance of changing the chemical state of the keratin and making it unsuitable for growth of M. audouini. It may have altered the progress of the disease, but the infection has not cleared up entirely.

Dr. Peck made an interesting point in his comment on the experiments at Zurich, and I believe the matter should be clarified. First of all, M. audouini affects the scalp first and only later involves the hair. In answer to Dr. Sulzberger, the fungicidal action of a substance isolated from the hair of adults, found by Rothman, takes place in vitro. It is generally recognized that results in vitro do not mean much when applied to conditions in vivo. Investigations have been made recently in the laboratory of Dr. G. M. Lewis in relation to the fungistatic effect of hormones on various kinds of fungi, and it is interesting to note how high the fungicidal effect of certain hormones is in vitro. The therapeutic relations, however, are in no way comparable to the laboratory results. Dr. Goodman brought out an interesting point concerning the p_H of the skin. Dr. Vamos investigated the problem of the p_H of the scalp of children and of adults. The p_H of children is much higher than that of adults. Applications of estrogens and androgens in a few of our cases of infection of the scalp with M. audouini shifted the p_H toward the acid side.

DR. MARGARET KLUMPP: One would expect that at least infection with M. audouini would be less tenacious and easier to eradicate in an adult, but in this case it has not been so. There were localized spots, and we performed epilation on these with roentgen irradiation; the infection seemed to be eradicated and all fluorescence disappeared for some time, only to reappear. Since then the infection has resisted all the remedies at hand. We have also tried manual epilation, but the infection is about the same as when the patient first came in, over a year ago.

NEW ENGLAND DERMATOLOGICAL SOCIETY

Dr. Bernard Appel, M.D., *President*

G. Marshall Crawford, M.D., *Secretary*

Boston, Dec. 12, 1945

Leukemia Cutis. Presented by DR. JOHN G. DOWNING, Boston.

A 72 year old white man, T. E., is presented with a generalized dermatosis of seven months' duration. His eruption began as red pruritic papules on the face and head, soon spreading to the neck. Some time during the early stage of the disease, a cervical abscess developed, which was treated with penicillin. Later, the eruption spread more rapidly and became generalized.

This patient is a somewhat emaciated man who looks older than his years. There is a diffuse erythema of the skin with slight thickening and a fine scale. The forehead and neck reveal occasional large, indurated, dark red nodules, some as large as 1 cm. in diameter. The ears and the feet are moist with serous exudate and some crusting. The feet, ankles and legs exhibit an advanced degree of pitting edema.

A biopsy revealed changes suggestive of leukemia cutis. The hemoglobin was 13.0 Gm. The leukocytes of the blood numbered 20,000 per cubic millimeter. A differential blood smear showed 61 per cent polymorphonuclear leukocytes (including 11 band cells), 19 per cent lymphocytes, 16 per cent monocytes, 2 per cent myelocytes and 2 per cent metamyelocytes.

This man was given roentgen therapy by the spray technic of 700 r (in seven divided doses). The patient has also received radioactive phosphorus intravenously in a dosage of 15 millicuries. Several blood transfusions have been given. The response to therapy has been striking, and the point of presentation is the result of treatment with roentgen rays and radioactive phosphorus.

DISCUSSION

DR. JOSEPH F. ROSS (by invitation): A new form of radiation therapy was made possible by the development of the cyclotron and the production of artificially radioactive isotopes. Of the artificially radioactive isotopes, radioactive phosphorus has been the most widely used. Radioactive phosphorus has proved to be a satisfactory substance for the treatment of chronic leukemia and also appears to be effective in the treatment of leukemia of the skin.

Radioactive phosphorus is given by intravenous injection, dissolved in isotonic solution of sodium chloride, and is metabolized by rapidly growing leukemic cells just as ordinary nonradioactive phosphorus would be. Owing to the increased rate of growth of these cells, they take up phosphorus more rapidly than normal nonleukemic cells, and the radioactive phosphorus is thus concentrated in the leukemic tissue. There it liberates its radiations (beta rays, or electrons) directly in the tissue, probably actually within the nuclei of the tumor cells. These cells are destroyed by the radiation, and the progress of the leukemia is retarded.

In patients with chronic myelogenous leukemia treated with radioactive phosphorus, the leukocyte count has been restored to normal levels, the character of the cells noted in the blood smear has returned almost to normal and the concentration of hemoglobin in the blood has risen to normal.

Two patients with leukemia of the skin have improved remarkably after treatment with radioactive phosphorus. Cutaneous lesions have practically disappeared, the blood picture has resumed closer to normal characteristics and there has been considerable subjective improvement, including disappearance of pruritus.

This treatment is still in the investigative stage, but certainly merits further trial. Treatment with radioactive phosphorus has some practical advantages over roentgen ray therapy. It can be given by physicians in the office without the necessity of calling in a radiologist. It does not produce radiation sickness, and since the radiation is delivered directly in the tissue adverse cutaneous reactions are not encountered. Unfortunately, radioactive phosphorus is still expensive. If, however, radioactive phosphorus, a by-product of the uranium "piles" used in the production of the atom bomb, could be made available for use of physicians, treatment with it would soon be much less costly than roentgen ray therapy.

Sarcoma of Skin. Presented by Dr. Agnes Israelian, Boston.

E. A. is a 73 year old white woman of Swedish birth, on the front of whose left thigh a lesion developed nine years ago. This was a painless olive-sized swelling, which remained essentially unchanged until five years ago. Thereafter it gradually increased in size, and at some later date the patient discovered lumps in her left inguinal region. These nodes disappeared after three or four months, but the original lesion on the left thigh persisted, and several new ones have appeared near it within the last year. During the past two months, all lesions have become distinctly larger and have turned a reddish hue for the first time. Accompanying these developments, the inguinal lymphadenopathy has recurred. A nonproductive cough developed about a year ago and has persisted, accompanied with a loss of 20 or 30 pounds (9 to 13.6 Kg.) in weight. There has been no hemoptysis. The patient has had no known exposure to tuberculosis and denies symptoms which might suggest syphilis.

Physical examination reveals an elderly woman who appears to be in good health. The tongue is fissured, and the mouth is edentulous. The blood pressure is 140 systolic and 80 diastolic. The lungs are clear, and the heart seems normal. The abdomen is soft, and there is no demonstrable enlargement of the liver or spleen. Midway down the anteromedial aspect of the left thigh are five or six red firm nontender movable nodules imbedded in the skin. On the front of this thigh is a hand-sized area of deep induration without discoloration, to which the skin is attached. There is a chain of matted lymphadenopathy in the left inguinal region. There is bilateral enlargement of the submaxillary lymph nodes but no other detectable change in the lymph nodes. The terminal interphalangeal joints of all the fingers are somewhat enlarged.

Laboratory observations were as follows: Roentgenologic examination revealed nothing of note in the lungs except calcified lymph nodes at the left hilus. The bones of the hands, feet, pelvis, hip joints and thighs showed no abnormalities. Examination revealed the blood and urine to be normal. The protein elements of the blood were within normal limits. A biopsy specimen has been taken and the histologic section reveals sarcoma.

DISCUSSION

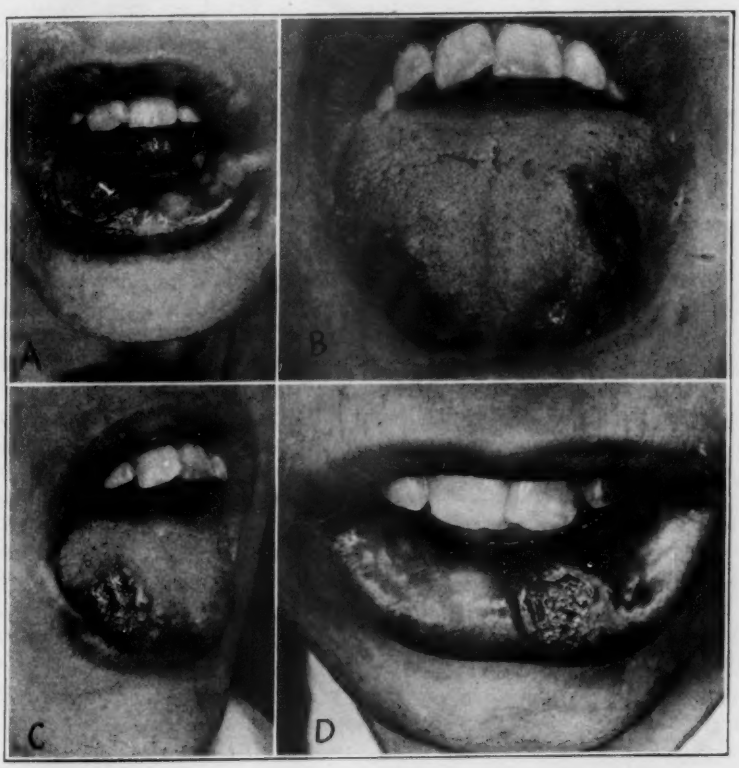
Dr. Francis P. McCarthy: I examined the pathologic section. It showed a massive neoplastic cellular infiltrate of lymphoid type. The number of eosinophils was relatively low. There were occasional large multinucleated cells suggesting the Sternberg-Reed type. Except for the history, this suggests Hodgkin's disease. The clinical history, however, does not conform to Hodgkin's disease of the skin. I would suggest removal of a lymph node for further study. When lymph nodes are in groups or chains, it is more suggestive of Hodgkin's disease.

Lupus Erythematosus. Presented by Dr. George Schwartz, Malden, Mass.

Granuloma Inguinale Involving the Corner of the Mouth. Syphilis. Presented by DR. GEORGE SCHWARTZ, Malden, Mass.

Ulcers of the Mouth ("Periadenitis Mucosa Necrotica Recurrens" or "Ulcus Necroticum Mucosae Oris"). Presented by DR. FRANCESCO RONCHESE, Providence, R. I.

A. D., a white woman aged 32, is presented with lesions at the mouth which had frequently recurred over a period of twenty-five years. The mucous membranes of the mouth, tongue and lips have all been affected. A fresh crop of



Various appearances and locations of recurring aphthous lesions during one year's observation in a 32 year old woman suffering attacks every one to three months for the last twenty-five years. Periods of freedom vary from one to three weeks. Lesions are fungating and almost resemble epitheliomas. Scarring following the repeated deep destruction of tissue over a period of years is evident.

lesions appears every one to three months, lasting several weeks each time. She may be free from lesions for as little as one week between outbreaks. The attacks come on rather suddenly, within a period of only a few hours.

There may be seen numerous deep ulcerations over the dorsum and sides of the distal third of the tongue, on the anterior halves of the buccal mucous membranes, in the gingival fossae and on the labial mucous membranes. These lesions are painful, and some of them are covered with a rather tenacious gray pseudo-

membrane. Interspersed among the active ulcerations are numerous depressed scars of past lesions. These have deformed the tongue to a considerable extent and are distinct on the lower lip.

The Hinton and Kahn reactions of the blood were negative. The nonprotein nitrogen was 30 mg., the cholesterol 180 mg. and the sugar 90 mg. per hundred cubic centimeters of blood. The hemoglobin content of the blood was 72 per cent, erythrocytes numbered 4,900,000 and leukocytes 6,700, with a differential count of 60 per cent polymorphonuclear leukocytes and 40 per cent lymphocytes. Examination revealed that the urine was normal.

Treatment has included administration of E. R. Squibb & Sons' "basic formula" vitamin preparation (thiamine hydrochloride, riboflavin, nicotinamide and ascorbic acid) by mouth, thiamine hydrochloride, U. S. P., subcutaneously, sulfapyridine by mouth, six vaccinations against smallpox (no reaction), Castellani's paint and 1 to 1,000 merthiolate locally. One autoinoculation with fluid from one vesicle was without effect. After the first three inoculations against smallpox a decided improvement was noted. Castellani's paint seemed to relieve the discomfort considerably.

DISCUSSION

DR. FRANCIS P. MCCARTHY: The term periadenitis mucosa necrotica recurrens is to be found in diagnoses in textbooks on dermatology and stomatology, but I do not believe that I have ever seen a case for which I used that terminology. I think that the necrotic type of lesion which this girl presents is a variety of severe aphthous stomatitis. The lesions on the tongue are deep and painful. She has had most of the usual caustic topical applications applied to the lesions. As a result of this local therapy she has some scarring of the mucosa. There is one lesion on the lingual aspect of the lower lip which represents an early aphthous ulcer. Scarring of the lip is rare in aphthous stomatitis. There may be a familial type of chronic aphthous stomatitis. I have seen 3 children in the same family with the disease, and the mother also had it. If it is a disease caused by a virus the patient should improve with several doses of smallpox vaccine. I would continue the vitamin therapy and give her solution of potassium arsenite plus calcium and iron preparation and smallpox vaccine. Combining all these remedies, I believe that results in this type of case may be obtained.

DR. WILLIAM R. HILL JR.: I had a patient who was treated with penicillin locally, but without improvement.

NOTE (Aug. 26, 1947).—Between January and May 1946 the patient received seventeen weekly inoculations with smallpox vaccine. She was seen in October and reported that her mouth had been completely free from ulceration for six months, which was the longest period of freedom from ulceration she had ever experienced. She was seen again in March 1947 when she presented one small labial lesion which caused little discomfort. Four additional inoculations with smallpox vaccine were administered in March. Up to this time (August 1947) the patient has complained of occasional discomfort, but no blisters or ulceration.

Mycosis Fungoides. Presented by DR. FRANCIS P. MCCARTHY, Boston.

Syphilis on the Tongue, with Monilia Organisms. Presented by DR. JOHN G. DOWNING, Boston.

A 73 year old white man, J. L., is shown with a complaint of sore burning tongue for the past nine months. This has at times been accompanied with burning of the entire mouth. The patient has been a tobacco chewer for years. The

Hinton reaction of the blood was positive in several tests nine months ago, but no treatment was administered because of the patient's age and the lack of other evidence.

The distal half of the tongue is distinctly shrunken and atrophic. The dorsum and sides reveal extensive geographic areas which are made up of grayish white leukoplakia. The latter is present also on the buccal mucous membrane. The remainder of the tongue is beefy red and smooth, except portions of the lateral aspects and the posterior dorsum, where there are small epithelial excrescences that suggest beginning degenerative changes.

Microscopic examination of scrapings of tissue from the tongue revealed clusters of sporelike bodies simulating organisms of the Monilia group. Cultures were on display which verified that impression. Roentgenographic examination revealed that the lungs were normal. There has been no treatment other than mild alkaline mouth washes, and the patient has improved symptomatically.

DISCUSSION

DR. FRANCIS P. MCCARTHY: This man has typical interstitial syphilitic glossitis. There is atrophy with leukoplakia on a bright red smooth tongue with absence of papillae and involvement of the oral commissures. The patient has verrucous epithelioma of the left oral commissure. There is also a lesion on the dorsum of the tongue of the verrucous type. Monilia often is observed in the oral cavity, but has nothing to do with the fixed lesions on the tongue and oral mucosa.

DR. ETHEL M. ROCKWOOD: I saw the culture, but it did not suggest pathogenic Monilia albicans. There was insufficient penetration of the mediums.

DR. JOHN G. DOWNING: We presented this case to illustrate the fact that the presence of Monilia in the mouth may be purely incidental. The organism in this instance was not M. albicans. It has been my contention that even if one does see M. albicans, it does not mean a great deal. If a pathogenic Monilia is observed on the skin, one should look elsewhere for a systemic disturbance, such as avitaminosis or tuberculosis.

DR. FRANCIS P. MCCARTHY: Routine cultures of the oral cavity of students in the course in bacteriology at Tufts Medical School showed from 3 to 5 per cent of the cultures growing yeast organisms of the albicans type.

Book Reviews

Atlas of Histopathology of the Skin. By G. H. Percival, M.D.; A. M. Drennan, M.D., and T. C. Dodds, M.D. Price, $16. Pp. 494, with 376 illustrations. Baltimore: Williams & Wilkins Company, 1947.

This book is a beautifully compiled atlas of histopathology of the skin, composed of 376 photomicrographs in color. They are the best colored reproductions using the Finley process that the reviewer has seen and the colors, even with special stains, are faithfully and accurately reproduced. The format of the book, including the arrangement of the text and legends, leaves nothing to be desired.

The authors state in the preface that they have attempted to portray in pictorial form the microscopic changes seen in the commoner diseases of the skin and, therefore, that the text matter has been severely limited to a brief explanation of the process illustrated. They have followed a clinical classification, grouping diseases according to the primary cutaneous change. This leads to a classification somewhat different from that seen in most textbooks on dermatology or in those on dermatohistopathology. The terminology employed is also different in many places from that used in standard textbooks previously mentioned, and because of this it would seem desirable in future editions to increase the glossary of terms, on the one hand, and add further synonyms, on the other. The reviewer would take exception, for example, to the inclusion under the term "psoriasiform carcinoma" of Queyrat's erythroplasia and Bowen's precancerous dermatosis and to the description of them as basal cell epithelioma, which they are not. Furthermore, the terms "superficial epitheliomatosis" or "erythematoid benign epithelioma" (Little) are more commonly employed than "psoriasiform epithelioma." There are a number of dogmatic statements in the text with which I doubt the majority of dermatologists would be in accord. Thus, on page 75 the authors state, in regard to lupus erythematosus: "The disease is generally regarded as having a definite connection with tuberculosis and has affinities with the sarcoids and granuloma annulare." For the most part, however, both the text and the legends under the illustrations are concise and well done. There is, however, a tendency to be too concise in certain descriptions; for example, in the two sentences describing mycosis fungoides there is no mention made of clumping of cells or pyknosis or karyorrhexis of individual cells, which are among the diagnostic features of this disease.

A few of the photomicrographs, although excellent reproductions, are of too low a magnification to bring out adequately the features of the disease in question or to fit with the descriptions in the legends under them. There is a relative lack of balance in regard to the number of photomicrographs of various diseases, especially some that are diagnostic histologically. Also, many illustrations are sometimes devoted to rare diseases; thus, for example, there is only one photomicrograph of lupus erythematosus but three of "orf." (ecthyma contagiosum), seven of cutaneous leishmaniasis and five of keratoderma blennorrhagicum. There are only four photomicrographs of psoriasis, not including any of so-called pustular psoriasis or recalcitrant pustular eruption; yet there are twenty-one photomicrographs of various types of "eczema," none of which present any special diagnostic histologic features. In the text on tuberculosis, one notes that such forms as inoculation tuberculosis, scrofuloderma and erythema induratum are not illustrated. Whereas leishmaniasis, which certainly is uncommon in northern countries, is included, there are no histologic pictures of lymphogranuloma venereum or

granuloma inguinale, nor is mention made of other uncommon diseases, such as blastomycosis or allied diseases, which have rather specific histologic pictures, especially when the organisms can be demonstrated.

In the section on nevi there is a disproportionate number of illustrations of nevus sebaceus, and in the description of nevus cells there is no mention of *lames foliacées,* neuroid tubes or clear cells (cellules claires), even though they occur in a relatively small percentage of pigmented nevi. Figures 223 and 224, labeled a case of "nevus pigmentosus (melanoma)," show predominantly the features of verruca senilis (seborrheic keratosis, or what the authors refer to as "nevus senilis" or "seborrheic wart"). Judging from their third picture of this case, figure 225, there apparently were a few ordinary nevus cells, so that both diseases apparently were present. It is difficult to follow the author's concept that angioma serpiginosum is merely a variant of capillary angioma, nor do their illustrations, figures 286 and 287, fit well with the original or subsequent histologic descriptions of this disorder.

The authors state that the atlas is intended primarily for postgraduate students and those interested in special study of dermatology. Because of the briefness of the text and its variance from that of standard texts in terminology, on dermatology and on dermatohistopathology, the book cannot be recommended for undergraduate students. Despite the criticisms that have been made, the book is a valuable addition to the library of pathologists, including especially dermatohistopathologists, and should prove extremely useful and valuable to students of dermatohistopathology, provided, as the authors suggest, that they use the atlas in conjunction with standard texts. The colored photomicrographs alone are worth the price of the book. The book is outstanding and unique in that it is the first atlas on dermatohistopathology, let alone general histopathology, in which all illustrations have been limited to excellent photomicrographs in color. It is hoped that when the next edition comes out further illustrations of other dermatoses will be added and the text amplified and in certain places modified or corrected.

Penicillin in Syphilis. By Joseph Earle Moore, M.D. Price, $5. Pp. 284, with 58 illustrations and 52 tables. Springfield, Ill.: Charles C Thomas, Publisher, 1946.

Here is a timely and valuable book which should serve as a guide for penicillin therapy for all forms of syphilis. With penicillin gaining widespread usage it is fortunate that this monograph should appear to serve as a text for the proper mode of administration of penicillin and, what is more important, as a warning against errors in penicillin therapy.

Admittedly, no person or single group has had sufficient experience or time to gather adequate data on this vast subject. With that fact in mind, Moore has pooled the results of nationwide studies by forty-four groups and clinics, drawing from twenty-six civilian institutions as well as the medical services of the United States Army, Navy and Public Health Service rapid treatment centers.

This well organized book is divided into nineteen chapters, the first eight of which deal with the chemistry, pharmacology, toxicity and mechanism of action of penicillin. The reviewer feels that chapter 5 could have been shortened by deletion of material which is not pertinent to the subject. Some fifteen pages deal with the effect of penicillin on various organisms and the results obtained in the treatment of pneumococcic, streptococcic and staphylococcic infections. The author has drawn some implications applicable to penicillin therapy in syphilis from these studies which could well have been summarized in a footnote.

The rest of the text is written in concise diagrammatic style. Typical chapters are devoted to treatment for early syphilis, cardiovascular disease, prenatal infection, congenital syphilis and neurosyphilis. The information obtained from the results of careful study of all available reports is clearcut, specific and easy to understand. Less emphasis is placed on the use of penicillin in latent syphilis.

Moore has classified experts in syphilology into three groups. There is the middle group ". . . which takes the position that although present methods are in many respects unsatisfactory, new developments constantly occurring and new methods constantly introduced, it is nevertheless worth while to describe the best method of treatment now in use and to relate the attainable results." It is to this openminded group of physicians that this book will bring its maximum value. To all others who use penicillin for syphilis it is no less warmly recommended.

Modern Dermatology and Syphilology. By S. William Becker, M.D., and Maximilian E. Obermayer, M.D. Second edition. Price, $18. Pp. 1017, with 461 illustrations in text and 37 full color plates. Philadelphia: J. B. Lippincott Company, 1947.

The second edition of this useful textbook is larger than its predecessor by one hundred and seventy pages. The material has been brought up to date, and the chapters on dermatologic therapy, pigmentary dermatoses and trophic and deficiency diseases have been amplified. A chapter on tropical diseases has been added. The importance of functional factors in etiology and therapy and the value of viewing dermatoses as processes rather than as morphologic entities are stressed.

Each chapter is introduced by a section on orientation, and the subject matter is presented in lecture rather than in encyclopedic form, which enhances its value to students and general practitioners of medicine.

The chapters on occupational and industrial dermatoses and eruptions due to drugs include useful charts and listings of substances which are important in the production of dermatoses.

The subject of syphilis is covered in two hundred and ten pages and includes chapters on the social aspects of the disease and the public efforts to combat it.

The text is printed on glazed paper in two columns per page. The illustrations are excellently reproduced. A short bibliography is included at the end of each chapter.

This edition should receive a hearty welcome from postgraduate students and practitioners of dermatology alike.

HOWARD FOX

UNIV. OF MICH.